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# MODERN MEDICINE

## ITS THEORY AND PRACTICE

IN ORIGINAL CONTRIBUTIONS BY AMERICAN AND  
FOREIGN AUTHORS

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VOLUME III

DISEASES OF THE DIGESTIVE SYSTEM—DISEASES OF  
THE URINARY SYSTEM

*SECOND EDITION, THOROUGHLY REVISED*

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# PART I

## DISEASES OF THE DIGESTIVE SYSTEM

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### CHAPTER I

#### INTRODUCTORY DISCUSSION ON THE DISEASES OF THE DIGESTIVE APPARATUS

By CHARLES G. STOCKTON, M.D.

IN this introduction it is intended to discuss certain critical relations that may exist between disturbed physiological activity and structural changes as expressed in morbid processes. The subject is to be considered from several different aspects as divided in the succeeding headings.

1. **The Whole and the Part.**—We are accustomed to look upon digestion as the function of an extensive and complicated apparatus, but it is so intimately related with the functions of other parts of the body that it is difficult to draw lines of precise limitation beyond which it can be said digestion has no part and receives no reciprocal activity. We commonly speak of the digestive apparatus as including the alimentary tract and those important glands which contribute specific secretions to the advancement of digestion; but as absorption and assimilation, on the one hand, and the formation and withdrawal of katabolic and waste products, on the other, are immediately related to the preliminary digestion, it is impossible to form a clear conception of the diseases of the digestive organs without taking into consideration the state of other and contributing parts of the organism. While it makes for simplicity in description to exclude from implication those organs not commonly grouped with the digestive apparatus, this does not result in a correct understanding, and, therefore, if one is to find an explanation not only for a disturbed physiological state, but also, in instances, for structural changes in the digestive organs, he must widen the field and direct his study to the nervous system including its psychical manifestations, to the fluids of the body, to the blood pressure, the metabolism of the tissues, and to the state of the emunctories. The importance of these matters is perhaps unconsciously recognized when we declare that good digestion depends upon restful sleep, fresh air, sunlight, physical exercise, and the proper activity of the bowels, kidneys, and skin. When we disregard these essential matters, it is difficult to form a just conception

of the nature of digestive disturbances, or to prescribe successfully therapeutic measures for their relief. For this reason one may truly say of a given dyspeptic, the trouble arises in the brain, or in the lungs, the heart, the kidneys, etc. The pathology of stomach diseases is not limited to that organ, but is the expression there of disturbances that may be widely distributed through the whole body. This fact applies to other parts as well as to the stomach. Answering Virchow's question, "Where is the disease?" we have sought to give each disease a local habitation, but this is only a relatively justifiable conception as regards any disease, although more true of some than others. There are probably no diseases referable solely to the kidneys, the heart, or the blood; the man is sick, and it appears here or there.

Although a large proportion of the affections of the digestive apparatus are functional, many cases with which we are confronted present an association of functional and structural abnormalities. Congenital malformations, displacements of abdominal viscera, and hernia, both internal and external, are structural defects; the infiltrations like amyloid disease, the more specific infections like cholera, typhoid fever, amœbic dysentery, and tuberculosis must be regarded as beginning their effects upon the body through their action upon its structure. But almost immediately these lead to functional disturbance, both local and general, and therefore the state of general vitality of the patient conditions the functional activity of each organ, and is a potent factor in the outcome of any local disease.

Many facts relating to digestion have come into our possession during the past twenty years, but the mere accumulation of facts and their presentation in isolation is not the most satisfactory method of studying a subject. By what laws are these facts related? In what is the favorable activity of one organ dependent upon that of another? Of the various links in the digestive chain, which are the more indispensable? If we shunt the action of certain parts through surgical intervention, what will be the final result in the organism? These are questions of vital importance, and by arranging our data with a view to answering such inquiries we throw most light upon the subject as a whole.

**2. Individuality in Disease.**—It is necessary to value carefully the individual equation. On the one hand misconception may arise when generalizations are based on the manifestations of a single case. On the other hand the question of individual peculiarity and idiosyncrasy must be carefully weighed, so that we may avoid the feudality of classification and the tyranny of established rule. For instance, von Noorden has shown that certain starches are comparatively successful foods in particular diabetics, although quite the reverse is true in other patients with this disease. Through idiosyncrasy the eating of potatoes or the flour of certain grains, although usually acceptable, in an occasional individual invariably excites intense gastro-intestinal distress. This action of certain foods is explained probably by the theory of anaphylaxis. Idiosyncrasy applies to other matters than food. The sensitiveness of some persons to the ill effects of mental excitement, physical fatigue, or exposure to cold must not be overlooked, nor must it be cast into a rule.

3. **The Interrelation of Digestive Functions.**—Common experience has taught us that the mental state and the sense of taste in some unknown way affect the primary digestion. Thus worry induces leanness, and happiness favors the opposite condition, in a measure independently of the amount of food taken. Some of the steps by means of which these effects are obtained are explained by the work of Pawlow. The digestive secretions and the motor activity of the stomach and intestine are excited by proper psychical stimulation. Distress may either inhibit or overexcite. Hirsch and von Mering have established the fact of an intimate relationship between gastric secretion and motion, and the secretions of the duodenum, pancreas, and liver. The presence of acid gastric juice in the duodenum leads, through reflexes arising in the latter, to the closure of the pylorus, preventing temporarily a further escape of gastric contents. This gastric juice within the duodenum, until neutralized by those secretions, stimulates the secretion of pancreatic juice, bile, and succus entericus; thereupon the pylorus again opens and the rhythmic movements of the stomach expel a further portion of the gastric juice into the duodenum, which, in turn, leads again to the closure of the pylorus. This reciprocal action demonstrates the important relation of one part of the digestive apparatus with another. Bayliss and Starling have shown that the presence of acid gastric juice in the duodenum stimulates the secretion of secretin, a substance which, passing into the blood and reaching the pancreas, excites in that organ its specific secretion; so it would seem that the intermittent and regular discharge of acid gastric juice into the duodenum is indirectly the normal stimulus of the pancreatic secretion. Trypsin, which was formerly supposed to be a secretion of the pancreas, has been shown by Pawlow and his students to be the result of the action of a substance found in the succus entericus, known as enterokinase, acting upon trypsinogen, which is secreted by the pancreas.

Attention has been called to the fact that psychical conditions may influence salivation and gastric secretion; then there follows stimulation or depression of the motor activity of the stomach and intestine, of the secretions of the duodenum, the pancreas, and the liver, and finally, the formation of at least one substance that activates the secretion of the pancreas and other organs which otherwise would remain relatively passive.

The impulse starting in a psychic state does not end in its effects upon the liver and pancreas. The functional activity of the small intestine is greatly influenced by the presence therein of the right proportion of secretion from the liver, pancreas, and other glands, and intestinal digestion would suffer in case of decrease or derangement in this supply. Under such conditions irritation of the intestinal mucosa, disturbance of its motor function, and lowering of the resistance of the part would result. With such a state of affairs it would be expected that bacterial life, especially within the gut, would be multiplied, fermentation occur, and infection be facilitated.

With physiological economy, there goes on in health the absorption of biliary salts and probably other substances by the intestine in order to



maintain a proper balance of the organism. When there exists a marked disturbance of intestinal digestion we have reason to suppose that it interferes with this absorption. While the liver may be embarrassed through not receiving by way of the portal circulation the usual supply of recovered substances, it suffers at the same time because of the absorption of the products of putrefaction. It has been shown by Adami that living bacteria reach the liver from the intestine. When the liver is thus overtaxed, a general toxemia supervenes, the whole body is injured, and hemolysis is often exaggerated. There exists a remarkable, although somewhat obscure, relationship between the liver and the kidneys, and under conditions described renal elimination may be decreased or otherwise deranged. To these evils others may be added when the colon, suffering in turn, contributes to the general toxemia. Delafield has emphasized the frequency of chronic colitis as the result of interstitial nephritis, and others have recognized the injurious effects of colitis upon the kidneys.

Relatively great importance attaches to the pylorus, duodenum, pancreas and gall-bladder. A fuller acquaintance with the functions of these organs not only throws light on the clinical course of the digestive diseases, but serves to warn us that surgical intervention must take into account the possible harm from any great disturbance of the relations of these parts.

**4. Adaptability and Vicarious Action of the Digestive Functions.**—At the same time we are impressed by the facility with which one portion of the alimentary tract is able to dispense with the assistance which it ordinarily receives from another, and by the success with which nature adapts herself to the absence of the function of the stomach and of large portions of either the small intestine or colon. With complete atrophy of the gastric mucosa, or with the bile diverted through a fistula from its intestinal course, or with the pancreas made practically functionless through chronic inflammation, the patient may survive and maintain a moderate degree of general nutrition. The loss of the function of a single digestive organ may not be accompanied by as serious results as ensue from lowering of vitality in the apparatus generally, such as follows grave diseases of the nervous system, or the chronic intoxications and infections. The organism seems capable of sustaining almost in entirety the loss of function of certain of the digestive organs. Nutrition sometimes fails as the result of depression, affecting all parts of the apparatus at one time. But to reiterate, it would be a misapprehension to suppose that health can be perfect after the loss of function of any one of the important digestive organs, or after the removal of parts, as, for instance, the stomach.

**5. The Relatively Great Importance of Motor Functions.**—Our understanding of digestive diseases has been much advanced by a clear conception of the rôle of motion in health and in disease as compared with that of secretion. It appears to the writer that the importance of motor disturbances of the digestive tract is not yet fully recognized. We find that although Nature adapts herself more or less successfully to the absence or derangement of what would seem to be necessary secretion,



she immediately resents marked disturbances of motility, whether there is overexcitation or overdepression. Especially, we find that evil results are brought about by such interruption of motion as gives rise to stagnation of gastro-intestinal contents or the interruption of the flow of secretion from the great digestive glands. In the latter case the mischief is not alone from the retention of secretion but from the results of stagnation and from the infections and intoxications which are thereby entailed. In a sense it may be said that an exception exists in the instance of the large intestine, where, in event of chronic constipation, we observe a considerable stagnation without necessarily serious consequences. This may be explained from the fact that it is the function of the lower part of the colon to retain its contents, and therefore in constipation we have to deal merely with the exaggerated function, going on ultimately to disease. But even here we recognize the evil consequences that result in some instances from even moderate stagnation, for constipation in certain individuals is immediately succeeded by general digestive derangement as well as by important constitutional symptoms. This is especially true of those unaccustomed to constipation or those in whom there is inadequate activity of the lungs, liver, and kidneys. In relation to the kidneys and liver, this statement is likely to pass unchallenged by some who would doubt its applicability to the lungs, but we probably fail to recognize the full importance of elimination by way of the lungs. Sufferers from emphysema, chronic fibroid pneumonia, or continued pulmonary congestion, are strikingly relieved by timely stimulation of the skin, bowels, and kidneys. Doubtless this arises in part through forwarding the circulation and assisting oxygenation, but the practitioner may convince himself that the element of elimination must also be counted.

The studies of Cannon indicate that our conception of the nature of gastro-intestinal motion has to be revised, and it is probable that new light will be thrown upon certain digestive derangements as a result.

**6. The Nature of Functional Disturbances of Digestion.**—The nature of the so-called functional diseases is best apprehended by studying them along general lines such as those suggested. The tangled symptomatology is easily misunderstood, and, for a long time, the pathology and the pathogenesis for the most part evaded the clinician. So far as relates to the stomach, a better conception of the facts followed soon after Leube's adaptation of Kussmaul's stomach tube as an instrument of diagnosis. It was then seen that the state giving rise to a complex of symptoms formerly described as "indigestion" was not a single pathological entity, that it was in fact not one thing, but a varied derangement of gastric activity, the more or less direct result of irritation or depression of the autonomic and sympathetic nerves. Therefore, these functional affections were early divided into two classes: first, functional disease from excitation, and second, from depression. This division, though useful and at times helpful, is not so simple as it appears; for in not a few patients we may discover evidences of an irritative character at one time and of a depressive at another. Symptoms from excitement may not materially differ from those following depression, and both may be manifestations of physiological fatigue, whether arising from particular or general sources

of exhaustion. These different manifestations were soon divided into three classes and termed disorders of secretion, motion, and sensation. Now, while this is a natural and probably permanent step in classification, it must be materially modified and supplemented in order to make it of value in the understanding of the actual disease. True, we do occasionally meet with a disturbance that seems to be wholly motor, secretory, or sensory, as, for instance, cardiospasm or gastralgia; but, with few exceptions, we find a complex in which two or all of these divisions of symptoms occur.

The trend of events that make up a definite and more or less constant group is to be recognized, and the complex identified and named only after a careful study of the situation. This study must not be limited to the mere investigation of the functional behavior of the stomach. Commonly, the etiology of the trouble will be found in some remote and perhaps unexpected region, in some leak of general energy, if the expression is permissible, or in some undiscovered irritation of the nervous system. Thus a retroverted uterus, proctitis, or a displaced kidney may indirectly lead to important digestive disturbances, even more frequently causes of gastric asthenia are to be found with eye strain. This subject has been so widely discussed in America, and from so many points of view, that it is somewhat threadbare; yet its signal importance remains largely disregarded. Irregular or asymmetrical astigmatism is the visual defect most often responsible for the functional disturbance, but it is not always in astigmatism of high degree that the trouble arises. It is more commonly found in instances of moderate degree of astigmatism with axes differing in the two eyes, and especially in anisometropia. Although not limited to that period of life, the nervous disturbances following these visual defects are apt to appear after the age of maturity, and are especially active when the crystalline body begins from age to lose in pliability. We are indebted to Gould for insisting upon the reality of the matter.

Formerly our text-books referred to but few gastric disorders save the well-established structural processes. With the advent of newer methods of study there arose a tendency to multiply the number of gastric neuroses until the array of titles in a modern book on stomach diseases becomes bewildering. Undoubtedly much good has come from this minute investigation of functional disorders of the stomach. Among other advantages, it has added to our knowledge of the physiology, but now that so many years of conscientious work have been paid out and so many valuable facts have been gathered in, we are in an admirable position to review the material along the lines that experience and a sense of proportion would direct.

When this has been well done we shall doubtless agree that our conception of stomach troubles has undergone an absolute reconstruction since the days when text-books treated of "indigestion" and "flatulent dyspepsia;" but we shall admit also that there has been something of over-refinement in the classification, description, and management of the gastric neuroses. It is rather remarkable that this outgrowth of recognized gastric neuroses should have occurred during an epoch in which a basis in definite morbid anatomy was required of practically all diseases; and

at a time when if no structural abnormality was shown to bear a constant relation to a symptom-complex, the pathogenesis of that disease was held in doubt. Notwithstanding this, our assembly of nervous affections of the stomach, for which no morbid structural setting was found, was adopted into our nomenclature and was not disputed by most of our clinicians.

Hereafter, as now, we shall doubtless admit that this was a decided advance; but already we are discovering that we had in several instances misconceived the real meaning of the situation. In accepting the doctrine that we might have an array of motor, secretory, or sensory disturbances merely as the expression of a neurosis, we became too oblivious of the fact that this supposed neurasthenia might in fact rest upon some definite local disease that escaped detection.

#### 7. **Functional Disturbances in Relation to Structural Disease.**—

This oscillation of opinion that makes for a resting in the truth has come in part as a result of the surgical treatment of abdominal diseases. It was seen that after the removal of gallstones and the drainage or excision of the gall-bladder, not a few of the supposed neuroses promptly disappeared, and the physician who had rested satisfied with the diagnosis of hyperchlorhydria was disconcerted. Gastric derangement is now recognized as a common manifestation in appendicitis and other structural diseases of the lower digestive tract. We are aware that from such causes arise gastric hyperesthesia, hyperchlorhydria, and hypersecretion, besides the syndrome of transient pyloric obstruction with characteristic delay in emptying the stomach even amounting to food stagnation. This latter event may be encountered in cases in which there is no structural narrowing of the pylorus or duodenum, but merely a reflex or spasmodic affection of the pylorus, with or without coincident derangement of gastric secretion, but, necessarily, with serious digestive disturbance both in the stomach and duodenum.

We have long known that this train of events was a natural accompaniment of pyloric or duodenal ulcer. Now that cholecystitis, appendicitis, etc., are admitted as causes, there is difficulty in persuading some men to believe that pyloric spasm ever occurs as the result of a neurosis; on the contrary, they hold that there is always local irritation in the region of the pylorus. They affirm the local cause and leave the burden of proof with those who yet hold the position that there remains a proportion of cases in which the functional element is the only and sufficient cause. As the evidence in support of this opinion has a fitting application to other supposedly functional disorders, it may be profitably mentioned.

To begin with, only a neurotic origin has been able to explain a few of the reported cases of congenital pyloric stenosis. Then there is the analogy of spasm in the sphincter portion of other organs. The idiopathic dilatation of the œsophagus following cardiospasm which Meltzer has elucidated, is an example, to which may be added vesical and anal spasm, besides the involuntary contraction in laryngismus, vaginismus, etc. Still further evidence is found in the cure of these morbid contractions by measures directed solely toward calming excitability. Finally, the surgeons have learned the futility of attacking neurotic affections by



operative measures, for the symptoms not only continue, but often increase thereafter. That there may remain some hidden structural defect is possible, but, in the light of ascertained facts, improbable. Indeed, when we come to analyze the cases of pylorospasm secondary to a diseased gall-bladder, it will be found that some of them present no signs of former perigastritis nor extension of inflammation to the pylorus or duodenum. In these very cases, then, we must admit some indirect functional excitation, differing, it is true, from our conception of a neurosis but leaving something that morbid anatomy fails to explain. This functional nerve excitation may be comprised in the principle of increased reaction in certain individuals, or in any individual at some particular time, to stimulation in some instances of the nerve fibres of the vagus and in others to stimulation of the fibres of the sympathetic; that is, the possibility of a vago-tonic or sympathetico-tonic state requires consideration in the absence of structural explanation for the cause of spasm.

An unprejudiced view would seem to grant that a disordered nervous system may at times give rise to cardiospasm or pylorospasm, but the warning should be kept in mind that we should seek the cause in some marked irritation at or near the abnormal contraction.

**8. Structural Changes Resulting from Functional Disorders.**—Accepting the doctrine that many gastric disturbances arise from nervous causes with and without assignable irritation at some point remote from the stomach, the question occurs as to how far it is possible for structural diseases of the stomach to result from severe or prolonged insult to the nervous system. The belief has long been held that gastric atony and even dilatation may ensue from long-continued nervous depression. It is not difficult to explain gastrectasis as the result of pyloric or upper intestinal obstruction, but there is a large residuum of cases of dilatation in which no obstruction is found, and their origin is usually attributed to prolonged nervous depression and overtaxation of the stomach with resulting myasthenia. In this connection it is interesting to note the accumulation of cases of acute dilatation of the stomach following surgical procedures. These are not limited to abdominal operations or injuries, for there are well-authenticated cases which have developed after extensive injury to one of the extremities or joints, or subsequent to grave pneumonia, or accompanying acute tuberculosis or carcinoma. In a proportion of these cases a real obstruction is found, usually in the duodenum, occasioned by compression of the gut between the root of the mesentery and the spinal column, the result of dragging of the intestines downward which sometimes occurs in great relaxation of the abdominal wall. In a majority of cases no cause save nervous shock has been discovered.

An important lesson is to be learned from these cases. That gastric and duodenal dilatation can occur within a few hours, with manifestations so serious that death usually results unless proper intervention is resorted to, and that this can occur without any preceding injury to the stomach or other abdominal viscera, seems a striking illustration of the relationship that exists between innervation and the well-being of the digestive apparatus. Until autopsy becomes more general, we are not likely to

know what percentage of unexpected fatal terminations after surgical operations may depend upon this accident.

If acute gastrectasis can arise from great depression of visceral innervation, it is conceivable that depression of lesser degree and long continuance may result in atony; and if to this we add the element of overtaxation of the stomach from indiscreet eating, we may easily explain those cases of gastric atony which do not result from obstruction.

One who has had wide experience in the examination of gastric contents is aware of the striking influence which the state of the nervous system has upon gastric secretion. It is not uncommon to find instances of hyperchlorhydria which disappear as soon as the patient follows a quiet, orderly life. On the other hand, systematic rest, with consequent improvement in the general health, often leads to the return of normal secretion in hypochlorhydria. In many instances it will be found that the neurasthenic state that gives rise to the gastric symptoms may not depend upon inherited weakness nor upon general nervous exhaustion, but as before mentioned, rather upon the overfatigue of some particular part of the nervous system. Mere local treatment of the stomach unaccompanied by improvement in other directions is usually unsuccessful in inducing a cure.

One naturally inquires whether these long-continued disturbances of secretion may not lead to inflammatory and other lesions of the gastric mucosa. Gastritis has rightly been given extensive consideration in most treatises on stomach diseases, though according to the experience of some, its frequency is exaggerated. The disease is to be regarded as an infection of the stomach. One is impressed, however, with the truth long ago pointed out by Beaumont, that the recuperative and regenerative power of the gastric mucosa is remarkable, and we find that not only inflammation, but moderate trauma of the stomach, goes on to rapid repair, provided the general conditions are favorable. What is often regarded as gastritis is in fact a functional irritability of the stomach lining, a hyperesthesia gastrica, and not a true inflammation. In the extremes of age or when resisting power has been greatly reduced by long-continued fatigue, general infection, or great nervous depression, experience shows that gastritis is readily excited and that, when once present, it is likely to continue until the general health is improved. This is also true of the gastric neuroses, and just as hyperesthesia and motor irregularity may be caused and continued by systemic depression, so also may this be true of gastritis. Apparently a good deal of confusion exists in the mind of the average practitioner as to when a case is inflammatory and when it is merely one of functional irritability. It is important to make the differentiation, but it is occasionally difficult, as also is the recognition of the etiological factors upon which either affection is based. While it is understood that a functional disturbance may arise as a result of nervous depression or excitement, that gastritis may depend upon such depression is not sufficiently recognized.

One must not dwell too much upon systemic depression as a cause in the development of gastritis; it is only a factor which predisposes to infection. It is commonly and justly believed that the toxemias also invite

gastritis. This probably results from a lowering of vitality in the gastric mucosa such as the intoxications may induce in other tissues. Local disturbances like acute constipation, hepatic congestion, and overloading the stomach are factors which generally aid in setting up this inflammatory reaction. The point should be made that while one person easily withstands indiscretion in diet, another immediately suffers from gastritis, and this is true because of the lowered resistance to infections which exists in certain individuals, a truth paralleled in infections of other organs; thus some individuals are predisposed to such infections as appendicitis, colitis, and cholecystitis.

**9. Structure and Function in Relation to Peptic Ulcer.**—In the search for the etiology of peptic ulcer we have discovered a number of other things, but not precisely that, and the ground has been so much tramped over that the boundaries of the question are considerably obscured. It is highly probable that though we include in one group cases found post-mortem, those produced experimentally, and those recognized clinically, they are not necessarily exactly the same thing. Gastric ulcer has been produced in animals experimentally by prolonged feeding on infected food. Inferentially, the same result would obtain in man; nevertheless, except when stagnation exists, the stomach with peptic ulcer is remarkably free of the usual evidences of infection. Virchow apparently solved the problem by the hypothesis of thrombus, and this cause has been shown to explain rare cases, though it apparently has no place as a cause in the great majority. A like conclusion attaches to the theories that gastric hyperacidity, lowered alkalinity of the blood, local trauma or the accidental manifestations of other diseases, like tuberculosis, syphilis, scurvy, or diabetes, are the direct and single cause. That the gastric mucosa may suffer ulceration like other surfaces of the body and from identical causes will probably not be disputed, but it is scarcely justifiable to regard all these instances as peptic ulcer.

If we consider the method of development of peptic ulcer we perceive two things, namely, gastric hyperacidity and lowering of vitality of tissue at a circumscribed point; we fail to account for the special cause that may explain the devitalization of tissue at these points. We should consider the following facts: (1) Classical acute peptic ulcer is prone to occur in chlorotic young women, and, although the exceptions are many, the rule must not be obscured. (2) Classical chronic or indurated peptic ulcer is prone to occur in men past middle age. (3) Peptic ulcer is prone to localize itself either at the lesser curve on the posterior surface near the pylorus, or in the duodenum. (4) Its tendency is to continue, to become chronic. (5) Some ulcers show immediately a design to perforate, others seem forever limited to the mucosa. In acute ulcer there is usually present an overactivity in the secretion of very acid gastric juice.

In reviewing these special features we recall unquestioned instances tending to nullify the rule; but too much weight should not be given to the exceptions in a subject holding so many possibilities of confusion; we should rather attempt to trace the usual lines more deeply, while at the same time noting and interrogating the unusual. After doing this



it would seem clear that in the gastric ulcer of the dead house we are dealing with several entities—differing in cause, tendency, history, and termination—although there are certain manifestations in which they are alike.

It would seem that there is some as yet unknown factor at work in the cause of true peptic ulcer, some factor which lowers the vitality of tissue, especially in certain regions of the stomach and duodenum. Apparently this factor is relatively common in early adult life in women, and after middle life in men, and in the latter is more disposed to chronicity. What is this factor? Will it be found in the local deficiency of antibodies, as suggested by Weinland? In local ischemia? In preceding lesions of neurotrophic nature, analogous to herpes or to the perforating ulcer of the integument? These questions remain unanswered, and the operative treatment of gastric and duodenal ulcer, while proving that the disease is more frequent than we were prepared to admit, and showing that, in men, duodenal peptic ulcer is seen about as often as gastric ulcer, has not materially aided in explaining the nature of the process. The hypothetical disappearance of antibodies may well account for the loss of tissue, but how shall we explain the local deficiency in antibodies? May this not rest in the neurotrophic realm?

Whatever may be the exciting cause, we are reasonably certain that the increased activity of the gastric secretion and its overacidity contribute much toward the rapid evolution of the ulcer and toward its chronicity. The pain and gastric irritability are to be explained in part by the pyloric and gastric spasm and by the delay in the onward passage of chyme. Thus, the rationale of the usual medical treatment by rest, diet, alkalis, local sedatives, and external applications is made evident. When failure follows this treatment, the result would seem to be attributable largely to the fact that it requires the utmost attention and pains to prevent interruptions in the course of treatment, and that a short interruption may prove sufficient to overcome what has been gained by days of patient effort. Whether food is denied or in proper form is given frequently and persistently, the idea of keeping the gastric acidity low and overcoming the element of spasm must never be forgotten; even after gastro-enterostomy done to procure drainage, the benefit resulting from a modified diet and a lowered gastric acidity is of considerable importance.

By a control of the functional activity of the organ we are able to modify the course of the structural disease. Of course, this principle is not limited to gastric ulcer, but illustrates the important and persistent interrelation that exists between organs and functions. Perhaps we should be more earnest in tracking structural diseases to a starting place in functional derangement, to the finding of lowered resistance in some areas of tissue as the result of biochemical deficiency, possibly neurotrophic in its inception. All this may strike some men as lacking the evidence of acknowledged experience, but such a decision would be premature. There are many facts to be marshalled in its support. The bizarre and rather unaccountable manifestations grouped by Osler under the head of Angioneurotic Edema should be recalled as an illustration of visceral lesions apparently secondary to neurotrophic disturbance.

We observe herpes facialis, sometimes persisting for weeks, appearing in some individuals whenever the health is depreciated by fatigue or other general causes. Such eruptions are prone to attack a certain area, reappearing in the same place and occasionally accompanied by severe pain. We occasionally observe perforating ulcer of the arm or leg persisting indefinitely, resisting topical treatment and recurring after excision. We should recall Raynaud's disease and also the curious non-traumatic hematoma auris, particularly observed in the insane. Marked subcutaneous extravasations of blood appear in certain neurotics in various parts of the body, disappearing, then recurring after a period of health. In one patient the writer observed this at intervals during several years; the attack sometimes alternated with, sometimes were accompanied by, the classical symptoms of gastric ulcer, and occasionally by hematemesis of grave character. In erythema multiforme one may observe the wide involvement of the mucous membrane, and one severe case was observed in which this disease was accompanied by the symptoms of gastric ulcer. This collection of presumably neurotic affections associated with structural lesions shows an indubitable relation between the nervous system and the integrity of tissue.

We have insufficient experimental evidence to prove that either a nerve lesion or a neurotrophic disturbance is a frequent cause of peptic ulcer, but the behavior of the affection strongly suggests the possibility. These statements are intended to emphasize a principle that seems to be too little recognized, that of the very close relationship existing in all parts of the organism between the structure and the functions which utilize that structure. It is true that we often find a structural change to explain the supposed functional disturbance, but it seems equally true that the functional disturbance may be the forerunning etiological factor in, sometimes the cause of, the structural disease.

The hyperchlorhydria so commonly present in peptic ulcer is often intensified by food retention, secondary to pyloric spasm, and the same cause is responsible for some cases of that condition usually called gastro-succorrhœa. However, there are cases of excessive secretion in which hyperchlorhydria is not dependent on spasm. It was long believed that this might be produced by local stimulation occasioned by the open ulcer. Pawlow's observations tended to discredit this view. He failed to excite gastric secretion in animals by irritation locally applied, although juice flowed freely at the sight of food and upon its introduction into the stomach. A highly acid secretion is made to flow in dogs as a result of faradization of the mucosa. Recently, A. Schiff has been able to excite the flow of gastric juice by local stimulation when the factor of psychic effects and the presence of food in the mouth or the stomach were eliminated. Clinically, we find that the acidity is increased by feeding and even by the suggestion of eating, as demonstrated by Pawlow. But we also know that hyperchlorhydria is present in gastric ulcer even when the patient is fasting and when the psychic influence is wanting. It is probable, therefore, that gastric secretion is excited by the irritation of an ulcer as well as by the suggestion or presence of food.

One may conclude that there is usually an excessive secretion and at



times retention of gastric juice in this disease, and there can be no doubt of the unfavorable effect of the hyperacidity in the course of the ulcer. Further, we know that chlorosis, so often associated with ulcer, is generally accompanied by hyperchlorhydria, and that an impressionable nervous system at least predisposes to the oversecretion.

10. **The Question of Secretion.**—The behavior of the stomach in the matter of secretion presents a problem not yet elucidated. By the action of certain proteins upon the mucosa of the pyloric end of the stomach there is excited in the glandular structure of the part a substance which passes into the general circulation, returns to the gastric mucosa, and excites therein an active secretion of gastric juice. Pawlow and Popielski have shown that this secretion occurs after the destruction of all nerves connecting the stomach with the ganglionic centres. Edkins has shown that it is not the result of a local reflex in the gastric walls, but is owing to a chemical influence, in mode of action similar to that of secretin and other so-called hormones or internal secretions. It is interesting to discover that the secretions of the stomach are governed by influences other than psychic or reflex nervous mechanisms. The facts lead us to conclude that gastric secretion may be stimulated by psychic influence, by direct stimulus occasioned by food in the stomach, and, finally, by the specific action of some chemical substance formed in the pylorus and acting through the blood upon the remaining portions of the mucous membrane of the stomach.

We still await the application of these physiological findings to explain certain conditions observed clinically. Although many cases of so-called gastrosuccorrhœa are in reality but instances of retention, there remains a group exempt from stagnation, but in which, although the stomach is washed out at bedtime, there is found a considerable amount of gastric juice present in the fasting stomach in the morning. Sometimes the secretion is so excessive as to lead to morning vomiting; in contrast is achylia gastrica, in which no secretion whatever can be discovered. Some patients who suffer from hypersecretion suddenly, and so far unaccountably, experience a diminution or suppression of secretion; in other words, a patient who one day is an example of hyperchlorhydria, on the succeeding day or week will show a continued absence of hydrochloric acid free or combined. When gastric secretion is for a long time absent, we describe the condition by the term "achylia gastrica." This affection, frequently seems to be unrelated to any morbid change in the structure of the gastric mucosa. In prolonged cases the glandular structure undergoes atrophy, and restoration of secretion becomes impossible.

It would be easy to explain these cases by inflammatory or degenerative processes in the mucous membrane of the stomach, but such conditions are apparently absent in the early stages of a large proportion of cases. At times the disease is susceptible of satisfactory improvement following local stimulation and general treatment; but often the trend of the disease is toward permanent loss of function. Lacking the stimulus of the free hydrochloric acid, the pylorus does not contract firmly, and the unchanged gastric contents pass into the duodenum, sometimes very soon after the meal is eaten. In such cases the stomach will be found empty

an hour after the ingestion of food, or if the stomach tube is employed soon enough to regain the stomach content, it will be found to have undergone no digestive change except such as depends upon the action of the salivary ferments. Since we have come to look upon the proper quantity and quality of gastric juice as the normal stimulus of duodenal digestion and as the signal for secretion in the pancreas, liver, and intestine, it is difficult to understand how patients suffering from achylia gastrica are enabled to continue in fair health and with moderately good general nutrition. Such, however, is sometimes the case. Patients with achylia gastrica followed for fifteen years, while never well, are yet not materially worse than at the beginning of the observations. In some instances there was apparent improvement which coincided with pregnancy and disappeared as soon as the period of lactation had passed.

In health the amount of pancreatic secretion seems to be controlled by the stimulus received in the duodenum from the gastric juice, therefore a very acid secretion should excite a proportionately active duodenal and pancreatic secretion. On the other hand, a lowered gastric acidity should be followed by lowered secretion from the other digestive glands. While this correlation and interaction between the digestive secretions seem normally to proceed in an orderly way, there must occur some deviation from the principle in case of achylia; otherwise we should find the disease to be a much more serious one than it actually is. Starling shows that the secretion from the pancreas is induced through the action upon it of secretin and apparently without the intervention of nerve mechanism. While this seems probable from physiological experiment, it does not perfectly accord with clinical experience.

On examination of the stools of patients with achylia gastrica, although it is common to find that too great a proportion of the food is passed undigested, and although probably a certain amount of it has undergone disintegration through the action of bacteria, still it is evident that the patients digest and assimilate a reasonable proportion of food, as they are able to maintain their weight at a somewhat lower standard, and to develop a fair, although diminished, energy. We have in the recent accounts of the physiology of digestion an explanation of certain of the phenomena observed in achylia gastrica, but we are embarrassed in that they explain too much. In other words, we find that the victims of achylia gastrica suffer far less than should be expected.

It would appear that some of the secretions are activated through certain stimuli with which we are as yet unacquainted, otherwise it would be difficult to explain the comparatively good state of health which many patients enjoy subsequent to closure of the pylorus associated with gastro-jejunostomy.

It is interesting in this connection to consider the question of natural and artificial inhibition of peptic digestion. There are cases in which despite high acidity of the gastric content, depending upon free hydrochloric acid, proteolytic digestion does not proceed; something has blocked the digestive process. The explanation of this inhibition has been sought for in various directions. Apparently there are some natural causes of inhibition, perhaps depending upon the stomach itself through the

formation there of antibodies. But certain foods and drugs also exercise an inhibitory action on digestion. The albumoses, gelatin and maltose, for instance, have a definite inhibitory effect, while lactose and most carbohydrates have none. In certain instances the concentration of the gastric juice is found to interfere with the digestion of proteins as well as other foods, and when the secretion of the stomach is diluted the digestive process is apparently favored. These facts may account for the curious behavior of the gastric digestion often observed clinically; the total acidity of the stomach content may be high, the amount of free hydrochloric acid may be above the recognized standard, and yet digestion does not proceed. In reviewing the question Sailer concludes that, after attributing to certain foods and drugs the power of inhibiting gastric digestion, and admitting that the element of concentration under special conditions operates to produce a like effect, there remains a group of facts that may be best explained on the hypothesis of the presence of an antipepsin such as has been announced by Danielewsky and Weinland. This substance may have a rôle, not only in protecting the walls of the stomach, but also, in certain conditions, of inhibiting proteolysis in the gastric contents.

With long-continued absence of gastric secretion, a certain proportion of patients show very defective intestinal digestion. In other cases the intestinal digestion seems very satisfactory, and we are forced to conclude that besides the acid secretion of the stomach there must be some other agent that acts to stimulate the production of secretin. Whatever this agent may be, its presence is more manifest in some cases than in others, if we are to explain thereby the variations seen in the intestinal digestion occurring in cases of achylia gastrica.

Oil passing into the duodenum acts to stimulate the production of secretin with an efficacy second only to that of the acid chyme. Probably the fatty foods in a measure replace the gastric juice in setting the secretion into circulation in cases of achylia gastrica. There would seem to a clinical confirmation of this statement in the successful therapeutic use of oils in relieving the diarrhœa that is sometimes such a troublesome symptom in achylia gastrica.

Another important matter relates to disturbances in metabolism especially when this involves functional disturbances of the liver. Careful examination of the stools shows that there is a wide variation in the amount of biliary coloring matter discharged in the intestine. The study of the quotidian secretion of the bile, so far as can be judged by that which escapes through a biliary fistula, confirms the belief that at least one function of the liver shows considerable change in activity from time to time. From the evidence we may conclude that these temporary modifications of hepatic function are directly influenced through the nervous system, through psychic impulses, excitement, fatigue, or depression. Drugs have comparatively little effect on the secretion of bile, apparently more upon metabolic processes, but the state of the nervous system seems to be potent in this regard. The secretion of bile is stimulated by the administration of biliary salts and in a somewhat less degree by the taking of oils. In health the entrance of acid chyme into the duo-



denum excites the outflow of bile, a result apparently dependent upon the action of hydrochloric acid upon the mucous membrane of the duodenum, thereby leading to the production and absorption of secretin in the blood. It will thus be seen that the mechanism of the secretion of bile seems identical with that of the pancreatic juice. In each case it seems to require the presence of secretin carried through the blood to the organ in question.

**11. Infection in Relation to Digestion.**—The importance of recognized infection in the etiology of structural diseases of the liver and biliary apparatus leads to the suspicion that unknown infections of moderate activity have much to do with the variations of functional power of the liver that are commonly ascribed to other causes. It must be owing to an acquired or inherent resistance that the liver is not more markedly and frequently deranged than it is by the occurrence of an unwholesome condition of the gastro-intestinal tract. Clinical experience leads to the conclusion that the constant presence in the intestine of pathogenic microorganisms and other sources of intoxication, which may not materially disorder the economy, must be tolerated by means of some form of immunity. It is further observed that with unusual nervous depression this protective barrier of immunity becomes insufficient; the symptoms of toxemia result, and not infrequently those of infection as well.

Undoubtedly these manifestations are not confined to the liver, for we perceive similar occurrences in the parenchyma of the stomach and intestine in gastro-enteritis. It can scarcely be an error to infer that organs that are thus intimately correlated and thus largely influenced by the sympathetic and autonomic systems of nerves must react to untoward nerve influences; and under such circumstances, when, so to speak, "the guard is down," the infection most readily breaks through and intoxicants still further perturb the function. We may find illustrative examples most often in young children, as in the effect of fright, injury, or heat exposure.

**12. Visceral Blood Supply in Relation to Digestion.**—This resistance to disease on the part of the liver seems to be proportioned in a measure to the liberality of the blood supply, and fails when, from narrowing of the hepatic artery, the supply of oxygen is decreased. While it is impossible to measure the precise reponsibility of each fact that operates in the development of the morbid process, it is evident that weight must be given not only to that which circulates in the blood, but to the volume of blood as well; and it is for this reason that of late more thought has been given to the question of sclerosis in the abdominal aorta and its branches.

Years ago it was suggested that in case of unusually large and numerous inosculations of the branches of the portal vein with the systemic veins, a sufficient auto-intoxication to produce definite symptoms might result. The explanation of coma in hepatic cirrhosis was adduced as an illustration. The introduction of epiploxy enabled us to observe effects of such inosculations artificially produced, and it must be admitted that some justification is found for the claim that toxic effects may be induced in this way. Especially is this true before the organism has accommodated

itself to the change in the circulation, and presumably, also, when the portal blood is for any reason in a specially toxic condition.

Not alone the liver may be the victim of these vascular defects, but also the other abdominal viscera. Thus some forms of pancreatitis are to be explained, and not a few instances of that disease of multiple etiology, colica mucosa. Arteriosclerosis, aortitis, and peri-aortitis abdominis may be held to account for many degenerations, functional disturbances, and special symptoms of the digestive apparatus. Among the latter are included neuralgias, motor disturbances, and lowered secretion. In those free from structural disease of the vessels, troublesome visceral disturbances resulting from vasomotor excitation or depression may occur. Perhaps certain affections whose origin is attributed to perturbation of the nervous system, and which are called functional, are so in a different sense than that conceived. They may properly be charged to morbid conditions of the vasomotor centres.

This would seem to be true especially of mucous colitis, an affection that has been accounted for by many morbid processes, some of them opposite in nature, but all perhaps possessing in common the quality of excitement or depression of the blood supply through disturbance of vasomotor centres or through more direct influence, and hence leading to prolonged congestion or ischemia of the colon. What is true in this part of the intestine may well be so in other parts and other organs. Vasomotor disturbance is an old conception, long used to explain visceral diseases, and although this view has been carried to extremes, it has never been quite dislodged, and undoubtedly, in a proportion of cases, is a source of trouble.

Passive congestion of the abdominal viscera at once induces a lowered functional activity and later degenerative structural changes. At first there is depression of the specific secretions with an increased activity of the muciparous glands. The motor function of the stomach and intestine becomes hesitating, irregular, and feeble, discomfort or distress is experienced, digestion is delayed and imperfect, while an exuberant growth of bacteria leads to fermentation and increased toxicity of the gastrointestinal contents. A lowered resistance of the tissues favors the entrance of pathogenic microorganisms and the setting up of inflammatory changes of a low order which, with the assistance of an increased toxicity, account for the degeneration of the parenchyma and the successive ingrowth of connective tissue in the digestive organs in prolonged portal stasis.

**13. False Combinations of Secretion.—Disharmony.**—The interrelation of the secretions, the enzymes, and activating substances is complex but interesting. By conjoint action they apparently lead to amazing results, and some of these still remain incomprehensible. There are both clinical and experimental reasons for believing that disharmony in physiological reactions may result in profound disorder of the digestive organs and even in the most serious organic diseases. Perhaps no better instance of the latter can be pointed out than pancreatitis induced by experimental injection of the duct of Wirsung with bile or with artificial gastric juice. Undoubtedly certain cases of pancreatitis follow obstruc-

tion in the ductus choledochus at the ampulla and the escape of bile into the pancreatic duct. Possibly the more acute cases may ensue from the entrance of gastric juice into the pancreatic channels passing from the duodenum. This seems more probable in light of the work of H. U. Williams. He shows that gallstones may so far dilate the outlet of the ductus choledochus as to make easy the entrance of duodenal contents, including bacteria and chemical agents, which might thus find their way into the pancreas. These dramatic and antagonistic results of misplaced physiological secretions seem in part to be demonstrated by the relief observed to follow the drainage of the biliary tract in chronic pancreatitis. There are doubtless other instances of injury inflicted inside the redoubts and not by the enemy. Some of these we rather dimly perceive, others are undiscovered, yet we see their results.

**14. The Place of the Biliary Tract in Digestive Pathology.**—The gall-bladder is a prolific source of disease in the abdominal organs. A great proportion of diseases of the gall-bladder develop as the result of infection, a statement which applies with equal force to the various forms of cholangitis. Without entering into the discussion of the means by which microorganisms find entrance into the bile passages, we find them present there, and as a result, an inflammation of greater or less severity is often established. The more acute infections give rise to suppuration or necrosis of the gall-bladder, while the milder ones set up an inflammatory oedema of the lining mucosa, and thus embarrass the natural ebb and flow of bile. The lining of the gall-bladder is not destroyed, but is irritated, and, as a result, an excess of cholesterin is secreted and the changed condition of the bile contained in the gall-bladder leads to the formation of calculi, in the centre of which, if the stones are recently formed, colonies of bacteria are usually found. The conditions which seem most favorable to the enlargement of a biliary calculus appear to be a slight inflammation of the lining of the gall-bladder with temporary and recurring obstruction to the cystic duct. Under these conditions the stone is likely to increase by laminated formation, and its presence in an irritated gall-bladder may excite spasm of its walls, which induces the symptoms known as hepatic colic.

The inflammation of the biliary apparatus and the increased tension put upon it lead to more or less permanent changes in the parts, such as dilatation of the biliary canals, widening of the outlet of the choledochus, and inflammatory adhesions uniting the gall-bladder to the surrounding parts. Concurrent with these events there is usually much sympathetic disturbance of other viscera sometimes so marked as to distract attention from the original seat of trouble. With the biliary apparatus crippled future infection is facilitated, and recurrence of cholecystitis and cholangitis is frequent unless the patient acquires an immunity through improvement in the general health. Diathesis is an important factor in disturbing immunity and diathesis is closely related to metabolic peculiarity. When protein or carbohydrate metabolism is faulty, infection occurs more readily and in order to successfully oppose it special attention may be required as to diet and elimination.



15. **Some Peculiarities of Pancreatitis.**—As before stated there seems to be a definite relation between diseases of the biliary apparatus and pancreatitis. There is accordingly a belief that this disease, whether acute or chronic, follows upon the entrance of infectious microorganisms through the duct of Wirsung. While this is doubtless true in some cases, there are yet instances of acute hemorrhagic pancreatitis in which no infection is demonstrable, despite careful search. It is recognized that the destruction of the gland and the production of the fat necrosis of Balser, so often an accompaniment of the acute forms of pancreatitis, are definite results of autolysis of the gland structure through the action of its own ferments and the digestive effects of these ferments on the fatty tissues in various parts of the abdomen, and even (through the lymphatics) in other parts of the body. Hemorrhage into the substance of the pancreas occurs at times without trauma, inflammation, or other assignable cause. It remains one of the unsolved questions.

16. **Correlation of the Abdominal Viscera through the Vagus and Sympathetic.**—There apparently exists a relation between the suprarenal glands and the functional activity of the pancreas and liver. The appearance of glycosuria in instances of intoxication with adrenal extract seems to bear on this relation. The abdominal sympathetic and vagal nerves are associated closely with the function of the suprarenals as well as with that of the pancreas and liver. Meltzer found that when the cervical sympathetic ganglion was removed from animals their pupils dilated widely upon the instillation of adrenalin solution. Loewi, suspecting that inhibition of nerve influence might lead, through action upon the function of the liver, to hyperglycemia and glycosuria, and supposing this inhibition to be connected with the pancreas, practised the ablation of this organ. In the animals thus operated on there appeared the usual glycosuria, and, in verification of his hypothesis, when adrenalin solution was instilled in the animals' eyes marked mydriasis immediately appeared. Following this he applied adrenal solution to the eyes of 18 diabetic patients, and of these, 10 at once showed mydriasis. In 28 non-diabetic patients the reaction failed in all but 2. One of these proved to have obstruction of the duct of Wirsung, and the other had Graves' disease.

These results indicate that the functions of the pancreas, liver, adrenal bodies and kidney are closely related through the autonomic and sympathetic divisions of nerves.

Sialorrhœa, as a definite symptom of pancreatic disease, is largely discredited, yet its concurrence must be admitted, sometimes in pancreatic calculus, again in cancer of the head, and occasionally associated with transient glycosuria. The reality of so-called pancreatic diarrhœa should not be too quickly abandoned. By the study of the unusual phenomena we may dispel the mist that obscures the field wherein play some of the most incomprehensible vital processes.

17. **Splanchnoptosis and Overtension of the Peritoneum.**—The displacements of viscera contribute in several ways to derangements of digestion. Gastropptosis may interfere with the motor function of the stomach through increased traction upon its membranous supports, thus giving rise to discomfort as well as interference with the blood supply.

The results of displacement of the small intestine are less understood, but ptosis of the colon, including displacement of the cecum and the sigmoid, is not infrequently the source of symptoms and of disease. The shortening of the ascending colon, thus raising the cecum to the upper part of the abdomen, the displacement of the colon downward, the exaggeration of the flexures, and the displacement of the transverse colon downward so that it appears as a long loop, occasionally as a double loop reaching the pelvis, are among the dislocations. Jacobi pointed out that the sigmoid flexure in the fetus is relatively very long, and this disproportion occasionally continues beyond infancy, even to adult life. Another common defect is the extension of the so-called omega loop of the sigmoid to the right until it may reach the region of the cecum. This is occasionally associated with extremely sharp bending of the sigmoid. The displacements of the stomach and the colon are apparently more important than those of the small intestine; at any rate, they are better understood. From excessive angulation of the sigmoid, stasis and dilatation of the colon are frequently developed. This angulation is also a contributing factor in exciting sigmoiditis, and is a source of embarrassment in the treatment of that affection. It is not appreciated that incomplete hernia is often the cause of more or less continuous abdominal distress and sometimes severe pain which is experienced in regions somewhat remote from the point of irritation. This is seen in the very minute epigastric herniæ which frequently are found in the linea alba, and also in incomplete and unsuspected herniæ of the inguinal and femoral canals. As these symptoms have been repeatedly shown to result from external hernia, it is fair to presume that like results obtain from internal hernia. It is probable that some of the patients who have undergone repeated abdominal explorations, hoping for a discovery of the source of pain and other symptoms, are in fact suffering from unsuspected traction of some part of the peritoneum or intestine which is caused by hernia.

As vestiges of past inflammation, *adhesions* of one part of the peritoneum with another sometimes remain, and the unnatural traction thus induced may so far irritate the peritoneum as to occasion pain and, reflexly, considerable derangement of the digestive processes; or there may be sufficient adhesion of the intestine or stomach to embarrass peristaltic movement and delay the onward passage of the contents. The symptoms thus induced, while of little moment in the more phlegmatic, become important in those hypersensitive beings who are prone to have abnormal abdominal sensation, and in whom a harmonious physiological digestion is more often the exception than the rule. In such individuals relief is sometimes obtained by judicious medical gymnastics and psychotherapy, while surgical measures rather augment the complaint, either because of the new adhesions formed or because the attention of the introspective patient becomes more firmly fixed on himself.

According to Wilms, the pain occasioned by disease or irritation in the abdominal viscera is really produced by means of traction communicated to the mesentery. The cerebrospinal system of nerves, distributed to the parietal peritoneum, is the seat of most abdominal pain. Some think



that the splanchnic and pneumogastric nerves are not implicated, but that abdominal pain is excited only in the endings of the cerebrospinal nerves, distributed to the parietal peritoneum (Lennander). Traction upon the mesentery or upon the adhesions irritates these sensory nerves. Overdistension of a loop of intestine leads to stretching of the mesentery and indirectly to tension of the parietal peritoneum.

From this point of view it is easy to understand how pain may be excited in regions somewhat remote from the seat of mechanical pressure or tugging, as occurs in hernia, adhesions, and visceral displacements.

**18. Psychoneuroses in Relation to Digestion.**—Frequently an association exists between digestive disturbances and the more definite neuroses and psychoses. Long continuance of infection of the digestive tract inducing a lowering of the general nutrition, leads to depression or irritation of nerve tissue, and sometimes appears to be the exciting cause of brain disease and also adds to its continuance. This is shown by the marked improvement that follows an enlightened course of dietetic and other treatment especially directed to the betterment of primary digestion. On the other hand, the lowered vitality, induced by definite nerve disease, is almost invariably accompanied by digestive disturbance. Illustrations of this fact are observed when the nervous disease rests upon inheritance rather than upon long-continued nerve strain. It is probable that infection and toxemia are much concerned in these morbid processes, both nervous and mental. With a lowered resisting power, infection of the digestive tract is easily excited

Under these conditions the intoxications increase because of accompanying faulty elimination. It is commonly observed that victims of nervous or mental disease suffer from urinary inadequacy, and from depression of the other emunctories. To this may be added the element of faulty metabolism which succeeds upon disturbance of organs of internal secretions, as, for instance, the adrenals and thyroid. Enteroposis with atony and dilatation of the hollow abdominal viscera is frequently encountered in the neurotic and the insane. Besides, congestion and degeneration of the glandular structures often occur, including the liver and pancreas, as well as the secreting tissues of the stomach and intestine.

**19. Variations in the Intestinal Flora in Their Relation to Diseases of the Digestive Tract.**—The character of the intestinal flora, particularly that of the colon, is a matter requiring careful consideration. When patients are deprived of foods containing animal proteins, remarkable improvement is reported to follow the deliberate attempts to plant new orders of bacteria, the presence of which is antagonistic to those microorganisms more especially concerned in the putrefaction of animal proteins and the incidental production of toxic substances.

To recur to the question of motor insufficiency and imperfect drainage, the importance of which in the clinical course of digestive disease has been pointed out, the matter appears more conspicuous in the light of the bacteriology of the intestine. Indication for attention to this source of trouble may be found in the urine. While we know that certain urinary toxins are the products of metabolism more or less normal, and

hence depend upon the state of the cellular tissues, clinical observation and laboratory study reveal that, to a considerable extent, other urinary toxins develop in the intestine. The infections of the gastro-intestinal tract occur both with and without inflammation, but in either event they are accompanied by derangements of secretion. Subacute gastro-enteritis may be followed by degeneration of the glandular parenchyma and even by exudation into the muscular layers, followed by round-cell infiltration and subsequent motor weakness of the stomach and intestine.

According to Sir Arbuthnot Lane, the evil effect of imperfect colonic drainage, induced by the presence of kinks in, adhesions to, or deformity of the colon, extend to all parts of the economy. He would remove the cause of intestinal intoxication by resection of the colon. The results which he has obtained are very instructive to the clinician.

It is because of the similarity in the symptoms between functional derangements on the one hand and of infection and inflammation on the other that there has arisen the confusion in differentiating these conditions. The difficulty is not lessened by the fact that infection is prone to follow certain of the neuroses; in fact, they often co-exist. Lowered vitality of a part favors infection, and then there exists a causal relation between neurasthenia and appendicitis, colitis, or other inflammatory involvement of the digestive apparatus.

## CHAPTER II

### DISEASES OF THE MOUTH AND SALIVARY GLANDS

By DAVID RIESMAN, M.D.

A THOROUGH examination of the mouth by all available methods is of great value, not only in the study of diseases localized in or confined to the oral cavity, but also in the investigation of general morbid states. Examination of the mouth is, however, often neglected, probably because so frequently good general health is found associated with a wretched condition of the gums and teeth. But this fact should not make us indifferent to the importance of morbid conditions in the mouth as sources of general disturbance and as features of diagnostic value. A good deal can be learned by a simple routine inspection. The blue line of lead may clear up the diagnosis in an obscure case. The presence of pyorrhœa, ulcerative processes and abscesses may afford a clue to the etiology of chronic arthritis or a general septicemia. Pigmentation of the mucous membrane may suggest the existence of Addison's disease.

A proper study of the mouth comprises inspection of the lips, gums, teeth, tongue, floor of the mouth, salivary glands, and general buccal mucous membrane. In cases of disturbed taste, false teeth and plates should be removed to ascertain their condition and that of the parts with which they are in contact. The sensation of taste should be tested in the accustomed ways; the saliva should be examined as to its consistency, quantity, odor, reaction, and chemical composition. A bacteriological study of the mouth may prove useful, and should be undertaken when diphtheria or other specific process is suspected. Palpation may often aid inspection.

**Bacteriology.**—The mouth is the constant habitat of many bacteria, by far the largest number of which are harmless saprophytes; but there are some that possess pathogenic properties, which they display, either in the mouth or elsewhere, when suitable conditions obtain. If the care of the mouth is neglected, the number and variety of pathogenic and non-pathogenic bacteria increase. The bacterial flora of the mouth is of course derived chiefly from without, from the air, food, and drink; but when infective processes are active in the organs or parts communicating directly or indirectly with the mouth, the bacteria concerned in them may find their way to the oral cavity. Thus in pulmonary tuberculosis, tubercle bacilli may be deposited by the sputum in the mouth; and it has been shown by Biedl and Kraus that the salivary glands are capable of eliminating bacteria circulating in the blood.

Despite the fact that the oral cavity teems with bacteria, wounds about the mouth usually heal by first intention. This is to be explained by the



fact that the saliva is after all, as Clairmont<sup>1</sup> has shown, not a good culture medium for bacteria, although its bactericidal power is extremely weak.

Aside from individual differences, there is a natural difference between the saliva of the submaxillary and that of the parotid gland. In most animals the first furnishes a secretion that has only a slightly deleterious action upon bacteria; while parotid saliva is capable of inhibiting the growth of several species of organisms. Those of the pyogenic group seem to suffer most in that respect, especially if the secretion is artificially stimulated. When abundantly secreted, the saliva may become sterile.

The researches of W. D. Miller<sup>2</sup> have shown that there is a group of bacteria more or less peculiar to the mouth. Their identification, however, is not yet complete, as the majority have been found in stained preparations only, and have not been cultivated on artificial media.

The following are the most constant mouth bacteria:

*Leptothrix innominata* (Miller) occurs in all mouths in which a white deposit is found along the gum margin.

*Bacillus maximus* (Miller) is the largest of the buccal organisms and is found especially in dirty mouths. It is similar to the *Leptothrix buccalis maxima* (Miller), the difference being that the latter does not give the iodine reaction, and has segments of greater length; but it may be that the two are identical.

*Iodococcus vaginatus* (Miller), according to Migula,<sup>3</sup> is really a mixture of bacteria. *Micrococcus gingivæ* (Miller) is found in pyorrhœa alveolaris and also in healthy mouths. *Cladothrix buccalis* is found attached to the teeth and in carious dentine.

*Streptococcus brevis* is the most common species of mouth bacteria. By using it as a test, Gordon was able to detect contamination with minimal quantities of saliva, and to prove that during speaking, particles of saliva were dispersed a distance of forty feet in front and twelve feet behind him.

*Bacillus gangrenæ pulpæ* is found almost constantly (95.3 per cent.) in diseased pulps and in dental caries. It possesses the power of producing gangrene of the pulp and softening of the teeth. *Bacillus necrodentalis* occurs in deep layers of carious dentine. *Bacterium gingivitis* (Kruse) was found in the mouth during an epidemic of scurvy.

The other bacteria that have been found in the mouth, and which are more important from a clinical point of view, are *Staphylococcus pyogenes*, *Streptococcus pyogenes*, *Bacillus pyocyaneus*, and the pneumococcus. These are sometimes found in the mouths of healthy persons. Longcope and Fox<sup>4</sup> have shown that virulent forms of the streptococcus and pneumococcus are more common in the mouths of healthy persons during the winter months than at other times.

Friedländer's pneumobacillus, *Bacillus pseudodiphthericus*, and *Bacillus diphtheriæ* have also been found. The last is of course present when

<sup>1</sup> *Wien. klin. Woch.*, 1896, No. 47.

<sup>2</sup> *Die Mikroorganismen der Mundhöhle*, Leipzig, 1892.

<sup>3</sup> *System d. Bakterien*, ii, p. 218.

<sup>4</sup> *Bulletin of the Ayer Clinical Laboratory, Pennsylvania Hospital*, iii, 1906.

diphtheria exists; but it may also be found in a number of healthy children. Erich Müller<sup>1</sup> found it in 24 out of 100 children examined.

The *Bacillus tuberculosis* is present in the fluids of the mouth in persons suffering from laryngeal and pulmonary tuberculosis, when the sputum contains the organism.

The typhoid bacillus was found in the mouth in 50 per cent. of the cases examined by Purjesz and Pert.<sup>2</sup> Not only was it present in the early stages, but it was obtained as late as the fourth and eighth week of convalescence. The bacillus of glanders, the bacillus of rhinoscleroma, and *Bacillus lepræ* may be found in the mouth.

The *Bacillus fusiformis* of Vincent, according to its discoverer, is normally present in the mouth.<sup>3</sup> Its relation to ulcerative stomatitis is discussed farther on. It is usually associated with a spirillum or spirochete. A number of anaërobic bacteria have been isolated by Ozaki.<sup>4</sup>

The *virus of rabies* is present in the saliva of animals suffering from rabies.

*Spirochetes* are common in the mouth, but have not been sufficiently studied. They are often associated with fusiform bacilli; at times also with a curved, sausage-shaped organism that was originally described by Miller as *Spirillum sputigenum*. The *Spirochæta dentium* of Miller which was found by Koch in the covering of both carious and sound teeth, and by Migula in association with other dental bacteria, requires further identification.

### SEPTIC INFECTION OF ORAL ORIGIN

**Oral Sepsis.**—Caries of the teeth, alveolar abscess, and various forms of stomatitis, being bacterial processes, may lead to disease at a distance from the mouth in one of two ways: (a) By the absorption of toxins and bacteria into the blood stream; (b) by the swallowing of pus containing toxins and bacteria.

(a) It is not improbable that some cases of cryptogenetic sepsis, ulcerative endocarditis, etc., have their primary source in the mouth. The writer has seen a case of fatal septicemia due to dental abscess. Oral sepsis plays an important rôle in the etiology of many forms of arthritis. Bull states that in 172 cases of arthritis deformans in which special search was made for an infective focus, 141 (76 per cent.) had badly decayed teeth or had lost teeth.

(b) William Hunter<sup>5</sup> considers oral sepsis a factor of great importance in the pathogenesis of pernicious anemia. The swallowing of pus in dental cario-necrosis, in alveolar abscess, and in stomatitis leads to septic gastritis. The writer has looked in vain in a number of cases of pernicious anemia for evidences of oral sepsis, although he has noticed the glossitis to which Hunter calls attention. Yet whatever the results

<sup>1</sup> *Jahrbuch f. Kinderheilk.*, Band xliii, p. 54.    <sup>2</sup> *Wien. klin. Woch.*, 1912, p. 1494.

<sup>3</sup> *Ann. de l'Inst. Pasteur*, 1899, xiii, p. 609.

<sup>4</sup> *Centralbl. f. Bacteriol. u. Parasitenk.*, 1912, Orig. 62, p. 76.

<sup>5</sup> *Pernicious Anemia*, London, 1901, p. 200 et seq.

of suppurative and necrotic processes in the mouth may be, Hunter's insistence on the importance of combating them is entirely warranted. The general practitioner, as a rule, pays too little heed to the condition of the teeth. Wherever there are cavities, they should be cleansed and filled, if that is possible. Rotten stumps should be pulled out and replaced by artificial teeth. Not only will mastication and, indirectly, digestion be improved thereby, but possible sources of infection that may eventually impair the health are removed.<sup>1</sup>

**Offensive Breath.**—The unfortunate possessor of an offensive breath is seldom directly aware of it. Among the causes of the condition are lack of care of the mouth; mouth breathing due to the existence of adenoids, enlarged tonsils, or badly placed teeth; poorly fitting artificial devices; ozena, empyema of the antrum, tonsillitis, diphtheria (in the last the odor is characteristic); local diseases of the mouth, as the various forms of stomatitis, especially the mercurial form; scurvy and caries of the teeth. In most acute febrile diseases the breath is somewhat offensive; in typhoid fever it is quite peculiar. A rather characteristic offensive breath, according to Rolleston, is found in cirrhosis of the liver. It resembles the smell of dried and decomposing blood. It is probably due to a failure of the antitoxic function of the liver and the consequent passage into the blood of poisons generated in the alimentary canal. Hence, it is a bad omen.

A sweetish breath is common in chlorosis and in diabetes; the odor is fruity in diabetes with acid intoxication, also in the non-diabetic forms of the acidoses; a urinous odor is found in uremia; and a peculiar odor difficult to describe characterizes septicemia. A permanent offensive breath is found in diverticulum of the œsophagus and in certain cases of atony and dilatation of the stomach. The odor in the latter cases is probably disseminated by the expiratory air, the gases producing it being taken up by the blood and eliminated through the lungs. This is also true of some cases of cystitis with ammoniacal decomposition of the urine. An offensive breath is common in carcinoma of the larynx, in some form of bronchitis, in pulmonary tuberculosis when there are cavities, and in abscess and gangrene of the lung. A particularly repulsive fetor is sometimes due to putrid plugs in the crypts of the tonsils. In hemoptysis the breath has a somewhat sour odor. There is sometimes an offensive breath in menstrual disorders and after the use of certain drugs, as arsenic, phosphorus, the bromides and iodides. The offensive odor following the abuse of alcohol is more often due to fusel oil and other ingredients than to the alcohol itself.

**Treatment.**—Most important is the determination of the cause and its removal, if possible. In addition, the use of antiseptic mouth washes is indicated. Miller recommends the following:

R—Acidi benzoici . . . . .	gr. xc	( 6.0)
Ol. menthæ pip. . . . .	℥xv	( 1.0)
Tr. eucalypti . . . . .	ʒi	( 30.0)
Alcohol. absol. . . . .	ʒiij	(100.0)

<sup>1</sup> Rosenberger, *Infections of the Mouth, including Oral Sepsis and Dental Decay*, Philadelphia, 1911.



A very satisfactory wash is the liquor antisepticus of the Pharmacopœia; also the following:

R—Potass. chloratis . . . . .	5.0
Tr. myrrhæ . . . . .	5.0
Aquæ rosæ . . . . .	q.s. ad. 90.0

## DISTURBANCES OF SENSATION

**A. Disturbance of General Sensation.**—(a) **Anesthesia.**—This is usually of hysterical origin, and more often unilateral than bilateral. As a rule, it extends to all qualities of sensation. In the rare cases not due to hysteria, the lesion involves the superior or inferior maxillary nerve or the tympanic plexus, or is located in the cerebrum, in which case there is complete anesthesia of one-half of the body.

(b) **Hyperesthesia and paresthesia** (formication, pricking, tingling) are usually the accompaniment of local processes, as the various forms of stomatitis; but they may be due to hysteria or to lesions of the central nervous system. They may, especially paresthesia, be the precursors of anesthesia and paralysis.

**B. Disturbances of Taste.**—Abolition of taste, *agusia*, may be general or partial, persistent or transitory. Transitory agusia depends on local conditions, being common in dryness of the mouth, particularly when that is due to oral breathing. If partial, it may affect one-half of the tongue or the anterior or posterior portion. In agusia of the anterior third the lingual nerve or the chorda tympani is involved. In glossopharyngeal lesions the agusia affects the posterior portion of the tongue. Centric agusia, that is, agusia due to disturbances in the gustatory centre in the uncinate gyrus, is theoretically conceivable, but has not yet been demonstrated. Agusia may coincide with general anesthesia of the mucous membrane, such as is found in hysteria. Hyperagusia is practically seen only in hysteria.

*Paragusia*, or gustatory paresthesia, is common in hysterical persons and in the insane. It is also observed in some cases of facial palsy and in old cases of otorrhœa; in both of these it affects the half of the tongue on the diseased side. Sometimes the epileptic aura takes the form of an abnormal gustatory sensation. In persons with fever and in those suffering from gastric disturbances there is at times a total perversion of taste, on account of which tastes agreeable to them in a state of health become insupportable. The writer had under observation a man suffering from neurasthenia and moderate arteriosclerosis, who had constantly a sweet taste, for which no cause could be found. There was no diabetes and no abnormality in the mouth to explain it.

In the absence of febrile affections and peripheral nerve lesions, the prognosis in paragusia should be extremely guarded, as it may be a forerunner of mental trouble.

## THE LIPS

In a state of health the border of the lips is of a bright red color, which disappears on pressure, but returns instantly. There are marked

differences in thickness and in the amount of mucous membrane exposed. A moustache on the upper lip causes it to become thick and also a little elongated. A thick lower lip is characteristic of certain races, and is seen pathologically in myxoedematous idiots. The upper lip is thickened in the scrofulous.

The so-called *double lip* is a hypertrophy or enlargement not of the whole lip, but of the labial glands, which causes a projection between the teeth and the red portion of the lip. The appearance produced is as if the affected lip were doubled, hence the names "*lèvre double*" and "*Doppellippe*." According to Eddington,<sup>1</sup> it occurs in young men, and affects especially the upper lip. The writer has also seen it in a woman. A lip thus deformed is liable to become dry, cracked and ulcerated. The treatment consists in the removal of a strip of mucous membrane, including all the enlarged glands.

A change in the *shape* of the lips may occur as the result of long-continued mouth breathing. The lips are pale and flabby, the upper lip is shortened, the lower often thick and rolled outward.

Fissure of the lips is common, and occurs usually in the centre, but also at the angles. Fissures at the angles of the mouth, rhagades, are most frequently seen in congenital syphilis and in scrofula.

Changes in the *color* of the lips and of the mucous membrane of the mouth are common. The lips are blue or cyanotic on exposure to cold, in asphyxia, in pneumonia, in emphysema, in congenital and in some types of acquired heart disease, in mediastinal tumor, in rupture of an aneurism into the superior vena cava, in polycythemia rubra and in poisoning with coal-tar products. In one of the writer's patients an attack of enterocolitis was always preceded and accompanied by intense blueness of the lips. Pallor of the lips and oral mucous membrane is found in anemia, hemorrhage, chronic parenchymatous nephritis, and in aortic stenosis. It is not always a positive sign of anemia, as the blood may be fairly normal and yet the lips be pale. In conditions leading to inspissation of the blood, as in carcinoma of the alimentary tract, the lips may be of a deep red, almost maroon color. In diabetes there is at times a striking redness of the lips, which the writer has usually found associated with a similar condition of the ears. In jaundice the mucosa on the inner surface of the lips has a yellowish tinge, which becomes more noticeable if the blood is pressed out with a glass slide. Semmola and Geoffreddi<sup>2</sup> state that if a jaundiced patient forces his mouth wide open, two yellow streaks can be seen on the soft and a portion of the hard palate. In lead poisoning, in addition to the characteristic blue line along the gums, there may be flame-shaped, bluish patches on the inside of the lips. In the so-called blue-gummed negro, bluish or brownish pigment stains are seen on the gums, rarely on the inside of the lips. The presence of brownish patches on the inside of the cheeks, on the palate, or lips is an important diagnostic sign in Addison's disease.

Unnatural *dryness* of the lips occurs in fevers and in ordinary colds. In the former the lips and teeth are often covered with brownish crusts

<sup>1</sup> *Glasgow Medical Journal*, 1906, lxy, p. 81.

<sup>2</sup> *Twentieth Century Practice*, ix, p. 477.



PLATE I



The Blue Line of Lead Poisoning, with a Deposit of Lead in the Lower Lip.



called sordes, which when picked leave a bleeding surface. *Tremor* of the lip is seen in general paralysis of the insane, in alcoholism, in hysteria, and in typhoid and other long-continued fevers.

**Eruptions.**—The most frequent is the fever blister—*herpes labialis*, cold sore—usually found on the skin surface and red border. There may be but a single vesicle, more often there are several, which become confluent with the formation of reddish-brown crusts. According to Schamberg,<sup>1</sup> herpes simplex is most common in childhood and early life; 55 per cent. of the cases occurring between the ages of ten and thirty years. Herpes is an accompaniment of pneumonia, malaria, and cerebrospinal meningitis. It is comparatively rare in influenza, and exceedingly uncommon in typhoid fever. There is a belief among clinicians that the occurrence of herpes in pneumonia is a favorable omen.

Herpes is of infectious origin; but the cause is probably not a single specific microorganism.

**Treatment.**—Spirits of camphor freely applied in the earliest stages may abort an outbreak of herpes; the lesions when present may be painted over with tincture of benzoin—several applications are made and allowed to dry; they are repeated two or three times daily. When crusts have formed, ointments, such as cold cream, camphor ice, zinc ointment, etc., favor their early separation.

*Eczema* is common in the upper lip in children having acrid nasal discharges. Parasitic skin diseases may attack the lips.

**Inflammation of the Labial Glands.**—**Baelz's Disease.**<sup>2</sup>—This is a chronic disease affecting the mucous glands of the lips. It begins as an indolent swelling and gradually leads to ulceration, without causing either enlargement of the lymph glands or constitutional symptoms. It probably depends on a special infection, but is not syphilitic, although its appearance may lead to the suspicion that the patient has a labial chancre. There is usually an accompanying superficial catarrhal stomatitis. The disease yields readily to applications of dilute tincture of iodine.

**Tumors of the Lips.**—The principal tumors of the lips are angioma (hemangioma), lymphangioma, and carcinoma.

**Harelip.**—This is a congenital deformity, consisting of one or more fissures in the upper lip, resulting from an arrest of development. The fissure is not in the median line, but corresponds to the line of junction between the intermaxillary and superior maxillary bones. Harelip may be single or double. The treatment is surgical.

## THE MOUTH

### INFLAMMATION OF THE MOUTH

**Catarrhal Stomatitis.**—Catarrhal, simple, or acute stomatitis is a mild disease, characterized by redness and swelling of the mucous membrane

<sup>1</sup> *Jour. Amer. Med. Assoc.*, March 2, 1907.

<sup>2</sup> *Uma, Monats. f. prakt. Dermat.*, 1890, xi, p. 317.

and by increased secretion of saliva. It is produced by irritants acting not too violently, these being mechanical, thermic, or chemical; as food too hot, too cold, too highly seasoned, or too sour; alcohol, tobacco; sharp edges of decayed teeth, caries of the teeth, tartar, dentition, difficult or fruitless sucking, hare-lip, the use of pacifiers, etc., improper care of the mouth, badly fitting teeth, and mouth breathing. Catarrhal stomatitis is present in many infectious diseases, partly as a result of the same cause, partly because of decomposition of food in the mouth, etc. Thus it is found in scarlet fever, measles, typhoid fever, influenza, smallpox, and gastric and intestinal disorders. It is also present, either alone or as an accompaniment of other forms of stomatitis, after the use of certain drugs, such as mercury, iodides, lead, bromides, bismuth, and arsenic. In diabetes, nephritis, and cachectic states a more or less pronounced catarrhal stomatitis is often found. When the process is confined to the gums it is designated gingivitis.

**Pathology.**—Hyperemia, increased secretion, and proliferation of cells are the changes usually found. The ordinary mouth bacteria are present in augmented numbers.

**Symptoms.**—There is moderate pain, which is increased on the ingestion and mastication of food; infants and young children are apt to cry and to protrude the tongue; sucking is difficult. The saliva is increased in quantity and becomes sticky and pasty. The sense of taste is impaired; the appetite diminishes; and in children there may be fever and at times even emaciation. Examination reveals swelling and redness of the mucosa; the tongue is tooth-marked; the interdental processes of the gums are enlarged, red, and thickened. The mucosa is covered with a tough, whitish saliva, usually in patches. In severe cases the papillæ of the tongue are prominent and bloody at their tips (papillitis). The breath is offensive.

**Treatment.**—Aside from the removal of the cause, cleanliness is usually all that is required. Simple antiseptic mouth washes, such as a 2 to 3 per cent. solution of boric acid, sodium borate (2 to 3 per cent.), or potassium chlorate (1 to 3 per cent.) will suffice. If the gums are spongy they may be touched with glycerite of tannin (1 to 10), and a little tincture of myrrh may be added to the mouth wash. In infants, the mouth, after nursing, should be washed with sterile water and the antiseptic then applied on a pledget of cotton or linen.

**Aphthous Stomatitis.**—This is characterized by the formation of cream-white patches or plaques firmly adherent to and embedded in the mucosa. It is most common in children, but may occur in adults, especially in women at the menstrual periods, after parturition, and during lactation. It is rare before dentition, and increases in frequency with its beginning and up to the end of the second year. There is in some cases a marked tendency to recurrence.

**Etiology.**—The bacteriology has not been thoroughly studied; but Levy, in eight cases, found staphylococci, associated in one with *Oidium albicans*. Streptococci were not found. Faulty hygiene of the mouth, decomposition of food remnants, and the irritative influences of dentition are predisposing factors. Whether the disease is contagious has not been



definitely established; not infrequently it occurs in several members of the same household. Hirsch<sup>1</sup> believes trauma to be important.

**Symptoms.**—Aphthæ are small, round, or oval plaques or ulcers varying in size from that of a pinhead to 0.5 cm. in diameter. They form with great rapidity, are sharply circumscribed, and surrounded by a reddish, slightly elevated border. The favorite sites are the tip and edges and under surface of the tongue, the inside of the lips, and the labiogingival pouch. Their number is usually small, although at times new ones appear as the old ones undergo healing. Often two ulcers are located opposite each other on the gums and on the lip. The pain is usually intense, quite out of proportion to the importance of the affection, and interferes with mastication. Salivation is present, the tongue is coated, the breath offensive, the temper irritable; there may be a little fever. Reference has been made to recurrent aphthæ; in persons predisposed to them any trivial disorder of the general health may bring on an attack of aphthous stomatitis. Aphthæ do not lead to scar formation.

**Treatment.**—The digestive tract and general health must receive attention, only in this way can the tendency to recurrence be removed. The local treatment consists in the use of antiseptic washes and, if necessary, mechanical cleansing of the teeth by a dentist. The ulcers may be touched with caustic, preferably the solid stick of silver nitrate. Baginsky recommends the application of a solution of potassium permanganate (1 to 150). Hirsch advises tincture of iodine or a 10 per cent. solution of chromic acid. Alum is also useful.

A *confluent form* of aphthæ in children is described by du Pasquier.<sup>2</sup> It is a serious affection, and is either primary or secondary to bronchopneumonia, gastro-intestinal disorders, or one of the exanthems. The lesions may appear benign at first, but are rebellious to treatment. There is fever and emaciation; at times an infectious erythema appears and constitutes a grave symptom. The disease lasts from one to two weeks, and may terminate in bronchopneumonia or meningitis. There is also a fulminant form ending fatally in twenty-four or forty-eight hours after the appearance of the aphthæ. The most striking post-mortem finding is a fatty degeneration of the liver.

Bacteriological examination of the oral lesions shows a polymicrobism, various round and rod-shaped organisms and Vincent's spirilla being found. It is quite probable that this form of stomatitis and the ordinary aphthous form are two etiologically different diseases. An affection resembling aphthæ, but at times forming more diffuse whitish patches has been described by Mann<sup>3</sup> and by Schomerus.<sup>4</sup> In the lesions the pneumococcus was isolated in pure culture.

**Ulcerative Stomatitis.**—The term ulcerative stomatitis is loosely used to designate ulcerative conditions in general as well as a specific disease of indeterminate etiology. It occurs in children and adults, and is largely due to lack of care of the mouth, decayed and sharp-edged teeth, and in children to improper feeding. Crowding of the teeth is also an

<sup>1</sup> *Ueber die aphthöse Mundentzündung*, Inaug. Diss., Leipzig, 1904.

<sup>2</sup> *Rev. mens. d. mal. de l'enf.*, 1903, xxi, p. 353.

<sup>3</sup> *Münch. med. Woch.* 1909, p. 72.

<sup>4</sup> *Ibid.*, 1909, No. 4.

important factor, ulcers not rarely forming on the cheeks and gums from pressure by wisdom teeth. Poisoning with mercury, lead, phosphorus, and iodine is a predisposing cause, as are also infectious diseases, scurvy, etc. Older writers have described epidemic outbreaks of ulcerative stomatitis, especially in barracks; but the condition was probably a different one, in some cases perhaps foot and mouth disease.

**Bacteriology.**—In addition to the common pyogenic organisms, the fusiform bacillus of Vincent (Plaut-Vincent) is probably an important factor in the production of the disease. This bacillus is a polymorphic anaërobe, growing at 37° C., on serum-containing media. It is practically always associated with spirochetes, and is found in a great variety of affections, *e. g.*, ulceromembranous angina, hospital gangrene, tropical ulcer, mercurial stomatitis, scurvy, pulmonary gangrene, peribuccal abscesses, and noma. Both the bacillus and the spirochete stain easily with dilute carbol fuchsin. The latter has been cultivated by Mühlens.

**Symptoms.**—The process, which is almost invariably limited to the region of the teeth, begins at the margin of the gums. The gums swell, become dull red in color, and are covered with a veil-like haziness; subsequently they become yellowish and necrotic, bleed easily, and stand away from the teeth. In the early stages the swollen gums may in part envelope the teeth, while the interdental processes protrude as thick, red ridges. As the edges ulcerate the teeth become more and more exposed. By lifting away the gums from the teeth, ulcers may sometimes be discovered quite early on the dental surface below the free edge. The ulcerative process may spread to contiguous parts of the lips, cheeks, or tongue, and the teeth may drop out. Salivation is profuse, and the odor of the breath horribly fetid. Chewing and swallowing are difficult, and in children there is fever; even in adults there may be slight rises of temperature. The duration varies from a few days to several weeks, but as a rule is not more than ten days.

**Treatment.**—Removal of the cause is of prime importance. The teeth should have careful attention and the mouth should be cleansed with antiseptic washes, such as the liquor antisepticus or hydrogen peroxide. Internally potassium chlorate in small doses seems to be of much value, but it should be administered with caution, especially in children; its use should not be prolonged. In severe cases the employment of silver nitrate locally is helpful. Gerber<sup>1</sup> has found salvarsan useful in Vincent's angina. This would justify its employment in severe cases of ulcerative stomatitis due to the Vincent bacillus and spirochetes.

A few words may be devoted to *mercurial stomatitis* (salivation), a subvariety of the ulcerative form. Its mode of origin is not quite clear, but it is generally held that the mercury, by its reducing action, injures the tissues and in that way prepares the way for pathogenic bacteria. Some persons have an idiosyncrasy to mercury, and in them a single small dose, or perhaps two or three small doses, will produce salivation. Preëxisting diseases, such as chronic nephritis, cirrhosis of the liver, etc., favor its development. Infants without teeth and the edentate aged

<sup>1</sup> *Deutsch. med. Woch.*, 1911, Nos. 30 and 46.



are not liable to mercurial stomatitis. In grave cases death may ensue from extensive ulceration or gangrene and septic absorption.

The *treatment* consists in the discontinuance of the mercury and the use of antiseptic washes, as hydrogen dioxide (2 to 3 per cent.), and, internally, potassium chlorate, gr. ij to iv (gm. 0.12 to 0.24). Mikulicz and Kuemmel recommend iodoform paste or strips of iodoform gauze laid in the mouth and Bockhart<sup>1</sup> potassium chlorate in powder or in the form of a 50 per cent. tooth paste.

**Gangrenous Stomatitis.**—*Synonyms:* Noma; cancrum oris; Wasserkrebs (German). This is a comparatively rare form of infection of the mouth. Like hospital gangrene, which in some respects it resembles, it was more frequent in pre-antiseptic days. Its chief feature is a rapidly spreading gangrene involving the cheeks, gums, and alveolar processes. It is more common in childhood and in hospital than in private practice. Although occasionally an independent affection, it is, in the majority of instances, an accompaniment of or sequel to infectious diseases, such as measles, scarlet fever, diphtheria, typhoid fever, whooping-cough, pneumonia, malaria, and dysentery. In rare cases it follows mercurial stomatitis. The old view that it is caused by the administration of mercury has been disproved. It usually affects children between the ages of two and five years, and seems to be more common in the spring and autumn; in adults it is exceedingly rare. Some authors have reported cases of so-called idiopathic gangrene of the mouth, in which the disease set in spontaneously without any preceding illness on the part of the individual attacked.

**Bacteriology.**—Various bacteria have been either isolated in culture or found in stained preparations, but for none of them has the crucial test of reproducing the disease by inoculation been done. The most common organisms are the fusiform bacillus and the spirillum of Vincent. Streptococci, staphylococci, pseudodiphtheria bacilli, and perhaps true diphtheria bacilli and pneumococci are also found. Hellesen<sup>2</sup> isolated a Gram-positive, non-encapsulated diplococcus, which in animals produced a typical and specific necrosis of tissue.

**Symptoms.**—The cheek and lip become swollen and the overlying skin glazed, colorless, and hypesthetic; a small ulcer forms on the mucous surface, rapidly becomes gangrenous, and advances in depth and width until the integument is reached. If the latter also melts down in the gangrenous process, a perforation results. The hole may be small, or the gangrene may speedily involve nearly the entire cheek, the gums, and even the alveolar processes, so that the teeth are exposed and loosened. In the gravest cases, the tongue and palate may become affected. In rare instances, the gangrene involves the outer parts of the cheek and spares the mucosa. Noma is nearly always unilateral.

The constitutional symptoms are often strangely mild when contrasted with the local process. Fever may be present; when present it is usually of a hectic character, at least in the terminal stages. The odor is very foul; the submaxillary lymph glands are enlarged. The disease has a

<sup>1</sup> *Monats. f. prakt. Dermat.*, xxxiv, 1902, p. 113.

<sup>2</sup> *Jahrb. f. Kinderh.*, 1908, lkvii, p. 294.

very high mortality—from 75 to 80 per cent. The duration is from one to two weeks; recurrences have been noted. Death when it occurs is due to bronchopneumonia or to exhaustion, which in some cases is hastened by a septic diarrhœa.

**Treatment.**—Removal of the diseased tissue by the knife or Paquelin cautery under anesthesia, the wound being afterward dressed antiseptically, is the most efficient treatment. Destruction of the odor is best accomplished with formaldehyde, potassium permanganate, or iodoform. Diphtheria antitoxin has been employed in some cases, on the ground that the diphtheria bacillus was present; but it is quite probable that the bacillus was not the Klebs-Loeffler, but the pseudo-diphtheria bacillus. An abundance of food and alcoholic stimulation are indispensable.

Swoboda<sup>1</sup> described a gangrenous inflammation of the *tooth germ* in the newborn, causing a destruction of the gums, with subsequent sequestration of the crowns of the teeth in infants that are still far from the normal period of dentition. The cause is probably a septic infection, and the prognosis is always fatal.

**Thrush.**—*Synonyms:* Mycotic or hyphomycetic stomatitis; Soor (German); muguet (French). Thrush is a form of stomatitis characterized by the formation of whitish patches largely composed of the causative fungus, the *Oidium albicans*. It occurs chiefly in infants, rarely in adults.

The *Oidium albicans* of Robin is generally accepted as the etiological agent; although some authorities hold the *Saccharomyces albicans buccalis* to be the cause of the disease. The oidium is a pleomorphic organism presenting under two forms, (a) small, yeast-like bodies and (b) filaments, both of which are usually found together in the mouth. The virulence of the organism may be augmented by passage through animals. Although in the body the oidium probably elaborates a poison, none has been found in artificial cultures.

Rajat and Péju<sup>2</sup> have isolated two types of fungus, one in which the cells are of the average size of yeast cells and the other in which they are from six to eight times as large. The small-celled variety was present in all (70) the benign cases, that is, in those yielding promptly to treatment; the large-celled forms were present in 5 tenacious cases.

Thrush seldom, if ever, appears in healthy individuals; but chiefly in those whose vitality is impaired. In infancy trivial disorders may prepare the way—simple colds, slight intestinal disturbances; while in older children and adults, usually the aged, pneumonia, typhoid fever, and the exanthemata are the predisposing causes. In early life the epithelium is more easily penetrated; moreover, there is in the newborn, according to Grosz,<sup>3</sup> a tendency to a desquamative process producing a thin, grayish deposit, which favors the development of thrush. An acid condition of the saliva, normal in infants and in older children easily produced by fermentation of milk remnants, facilitates the growth of the fungus.

<sup>1</sup> *Die Therapie der Gegenwart*, 1904, xlv, p. 515.

<sup>2</sup> *Comp. Rend. Soc. de Biologie*, 1906, lxi, p. 523.

<sup>3</sup> *Jahrb. f. Kinderh.*, 1896, xlii, p. 177.

# PLATE II

FIG. 1



FIG. 2





PLATE III



Herpetic Inflammation of the Mouth and Tongue.





The too vigorous washing of the mouth practised by some nurses after the birth of the child may act in the same way. The disease is contagious and is transmitted by dirty nipples and dirty feeding bottles.

**Symptoms.**—The first sign is the formation of small, whitish points on the tip and edge of the tongue and on the inner surface of the lips, places on which desquamation of the mucous membrane is favored by the act of sucking. The points grow into patches of varying size, and may cover the entire inner surface of the mouth like a coat of plaster. In some cases the disease extends to the œsophagus and stomach; the nose and larynx may also be affected, rarely even the vulva. The patches consist of mycelial threads and epithelial cells, with leukocytes in small numbers. The mucosa is red and bleeds easily if the patches are forcibly detached. Nursing in infants and in older children deglutition and mastication are difficult. There may be slight fever and restlessness; an eczema of the buttocks is sometimes noted. Several writers have recorded cases of thrush metastasis.

**Diagnosis.**—All that is necessary is to examine a bit of the deposit under the microscope. Sometimes the patches are mistaken for curds of milk, which in appearance they closely resemble.

**Treatment.**—For prevention, pasteurization of the milk and cleansing of the bottles and of the mouth after feeding are important. Ordinarily, the disease yields readily to simple measures, such as wiping away the patches with a piece of soft linen or gauze soaked in boric acid or sodium bicarbonate solution, the mucous membrane being afterward brushed with the same solution, or with a weak solution of mercuric chloride (1 to 4000), sodium hyposulphite (1 to 25), or a weak solution of borax or potassium permanganate. Such constitutional treatment as is suggested by the underlying conditions must be instituted.

**Herpetic Stomatitis; Herpes Buccalis; Stomatopharyngitis Herpeticæ or Herpetiformis.**—Various herpetiform eruptions affect the mouth aside from the simple herpes of the lips. Some are associated with herpes of the pharynx; others are limited to the oral cavity, usually its posterior portion. In a case of the writer's, the vesicular eruption involved the tongue, lips, gums, and tonsils, and it was associated with a violent conjunctivitis. (See Plate III.) The vesicles were small, yellowish white, and on the gums became confluent. There was some fever, inability to swallow, salivation, and pain. The condition presented the picture of an acute infection. Only one culture was made, and that was negative. As pneumonia is an occasional, though rare, complication of herpes of the mouth and pharynx, the latter may, like the former, be of pneumococcic origin. In women a herpetic stomatitis sometimes occurs at the menstrual period.

**Treatment.**—This consists in the use of the milder antiseptic washes, as, for example, liquor antisepticus (1 part to 2 or 3 parts of water).

**Gonorrhœal Stomatitis.**—This occurs in the newborn from five to twelve days after birth, in the form of whitish patches on the anterior two-thirds of the tongue, leaving a free border from 2 to 5 mm. wide; also on the anterior half arches, and the posterior border of the alveolar process of the upper jaw, along the free edge of the gums anteriorly,

and occasionally on the frenum of the tongue and lips. A reddish reaction zone surrounds the exudate. The functional disturbances are slight, and the process heals without scars in from four days to four weeks. In adults it is rare. The cause in children is infection of the mouth with the gonococcus during birth.

**Treatment.**—Silver salts in dilute solution (1 to 2 per cent.), as a rule, bring about rapid cure; mercuric chloride (1 to 7000) may also be used.

**Bednar's Aphthæ.**—These are small, whitish plaques occurring in the newborn in the region of the hard palate. They are probably due to pressure of the tongue or the nipple during sucking, their development being favored by the general tendency to epithelial desquamation in the first few days of life. Baumm<sup>1</sup> considers the forcible cleansing of the mouth, practised after birth by some nurses, to be the real factor. The ulcers heal spontaneously as a rule; in rare cases they constitute the atrium of a general infection.

### TUMORS OF THE MOUTH

**Carcinoma.**—This may start in the mucous membrane of the cheeks, the gums, about the angles of the mouth, the lips, or in the floor of the mouth. It is usually of the squamous type, more frequent in men than in women, and very malignant. Early operation is the only treatment that promises good results.

**Cysts.**—The most common cystic tumor of the mouth is the so-called ranula (French *grenouillette*), which may arise from the sublingual gland or its ducts, from Wharton's duct, or from a small group of glands—the glandula incisiva—in close proximity to the neck of the middle or lateral incisor. In rare instances a ranular growth may take its origin from the remains of the thyroglossal duct, or from the branchial clefts, or finally, from Blaudin-Nuhn's glands on the under surface of the tongue. It is at times difficult in a given case to determine the origin of a cyst, but it may be remembered that those from the thyroglossal duct have a lining of columnar ciliated epithelium, while those arising from the acini or excretory ducts of the salivary glands have a lining that more or less faithfully reproduces the epithelium of the parent structure.

Suprahyoid and submental cysts are sometimes found associated with cysts of the sublingual region, with which they may communicate, but they may also exist independently. The ordinary ranula results from obstruction of the gland duct, and is in its nature a chronic tumor. An acute ranula has also been described; it is due to an acute inflammation of the duct of the submaxillary or sublingual gland, or of both. Cysts of the parotid gland are extremely rare. One with a lining like that of the mouth is reported by Morestin.

**Symptoms.**—The characteristic symptom of ranula is the presence of a cystic tumor on the floor of the mouth, usually just to one side of the median line, pushing up the mucosa, which is tightly stretched over it, and displacing other structures. Fluctuation is easily obtained.

<sup>1</sup> *Berl. klin. Woch.*, 1891, p. 840.

**Treatment.**—Evacuation of the contents is an uncertain method, unless combined with strong cauterization of the lining wall. The old-fashioned seton is still in vogue, and may give good results. In some cases excision is necessary.

A *dermoid cyst* on the floor of the mouth has been described by Brentano.<sup>1</sup> *Mixed tumors*, to be more fully described in the section on Salivary Glands, are also to be found in various parts of the mouth.

## DERMATOSES OF THE MOUTH

Various affections of the skin may simultaneously or independently affect the mucous membrane of the mouth.<sup>2</sup>

**Urticaria.**—In severe cases of urticaria, especially in giant urticaria, similar lesions may appear in the mouth. The tongue and uvula may be enormously enlarged; there is intense burning and thirst and at times alarming shortness of breath.

*Angioneurotic œdema* is characterized by a sudden painless swelling of the parts involved. The lips when affected, and they are a very common seat of the disease, are swollen to an enormous size and stand out as huge, stiff, fleshy masses. It is most common in women, and has a tendency to recur. Gastro-intestinal symptoms, especially nausea and vomiting, may be present, but are not constant.

**Treatment.**—The œdema tends to disappear spontaneously, and remedies seem to have but little influence over it. Benefit may be gained from calcium lactate, given in 10 grain doses (gm. 0.6) three times a day. If there is any disorder of the gastro-intestinal tract, this must be corrected, and the diet should be simple.

**Psoriasis.**—It is doubted by many whether psoriasis occurs on the mucous membrane. In the cases in which no lesions of the skin existed, the buccal disease was either leukoplakia or some other non-psoriatic condition. A probable genuine case is, however, reported by Oppenheim.<sup>3</sup>

**Lupus Erythematosus.**<sup>4</sup>—This invades the mouth from the face and usually presents itself as superficially inflamed areas, having an elevated, deep-red border marked radially by dilated veins; in the centre of the patches the mucous membrane is atrophic, violaceous, and dotted with countless fine white or bluish-white points or lines. Some of the plaques show erosion of the surface and are covered with a yellowish-white deposit that cannot be detached. In older foci the appearances may be somewhat different—the edges are less elevated, and usually have extending from them fine arborescent prolongations. The most frequent seat of lupus erythematosus is the cheek corresponding to the space between the upper and lower teeth. In the differential diagnosis, eczema, lichen planus, pemphigus, leukoplakia, and perhaps psoriasis have to be considered.

<sup>1</sup> *Deutsch. med. Woch.*, 1906, p. 164.

<sup>2</sup> Only the most important can be mentioned here; for a fuller account the reader is referred to text-books on diseases of the skin, particularly to Stelwagon, Schamberg, and especially the exhaustive work of Trautmann.

<sup>3</sup> *Monat. f. prakt. Dermat.*, 1903, xxxvii, p. 489.

<sup>4</sup> See the article of Kren, *Arch. f. Derm. u. Syphilis*, 1907, 83, p. 13.



**Treatment.**—This consists in counterirritant and absorptive applications and cauterization, but is usually of little avail. Unlike lupus vulgaris, lupus erythematosus is not greatly influenced by the x-rays.

**Lichen Planus.**—The lesions of the mouth are nearly always found in association with lichen planus of the skin; in rare instances they antedate the latter. They appear in the form of whitish dots, plaques, or streaks, giving to the mucous membrane an appearance as if it had been cauterized with silver nitrate. The lesions are unattended by any inflammatory reaction and may persist for years without change. The disease is most common in those whose nervous systems are depressed.

**Treatment.**—This in the main is general, the common tonics—iron, strychnine, quinine, and cod-liver oil—being the remedies indicated. Arsenic in ascending doses (up to 10 minims of Fowler's solution) is a valuable agent; mercury is also useful, especially in cases in which arsenic fails. Radium is worthy of a trial.

**Pemphigus.**—Pemphigus may appear on the mucous membrane of the mouth, the lesions being widely scattered over the gums, the roof of the mouth, and the soft palate. Farlow<sup>1</sup> reported two obstinate cases, in which successive crops of vesicles appeared. At various times lesions were also present on the cornea, in the nose, in the vagina, and on the leg. The *treatment* consists in the use of alkaline antiseptic washes to prevent secondary infection, and the administration of arsenic. Local anesthesia (cocaine, orthoform) may be necessary to render eating possible.

**Acne.**—This is rarely found on the mucous membranes. Unna<sup>2</sup> described a case affecting the upper lip, in a woman who had acne of the mouth and chin. The lesions yielded to treatment with resorcin ointment and ichthyol soap.

**Eczema.**—Eczema sometimes affects the vermillion of the lips.

**Tinea Circinata.**—This may spread from the face to the lips and mouth.

**Scleroderma.**—This sometimes attacks the mouth, leading to atrophy of the mucous membrane and to its adhesion to the submucous tissue. It may also cause falling out of the teeth.

**Erysipelas.**—In rare cases erysipelas of the face extends to the mouth, producing a deep redness and swelling of the mucosa, and profuse salivation. The soft palate and uvula are especially involved, and their swelling causes pain and difficulty in deglutition. In severe cases the tongue may be involved, as well as the pharynx and larynx. The diagnosis is only assured if erysipelas co-exists, or has immediately preceded or immediately followed. In persons having repeated attacks of erysipelas, groups of small vesicles are sometimes found in the mouth. They may be of the nature of lymphatic varices.

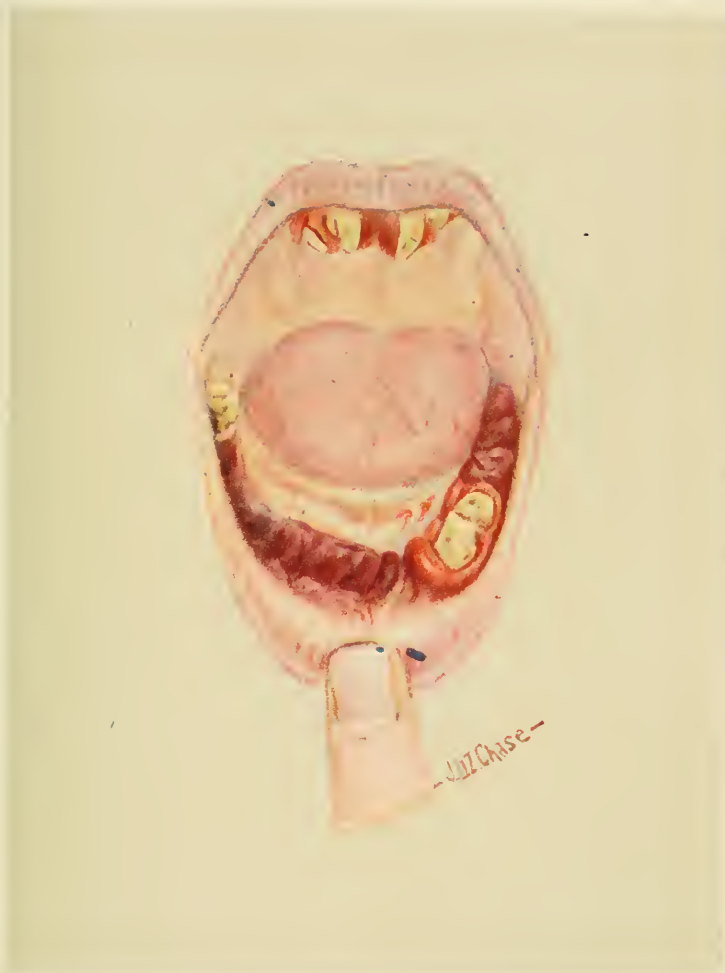
#### CHANGES IN THE MOUTH DUE TO GENERAL DISEASE

**Typhoid Fever.**—In addition to the familiar changes in the tongue, typhoid fever produces alterations in the mouth of a less well-known

<sup>1</sup> *Boston Med. and Surg. Jour.*, 1904, cli, p. 671.

<sup>2</sup> *Monats. f. prakt. Dermat.*, 1890, xi, p. 321.

PLATE IV



The Mouth Lesions in Scurvy.



character. These consist in ulceration, usually on the upper part of the anterior faucial pillar, on the tongue, uvula, cheeks, lips, and labio-gingival folds. Devic<sup>1</sup> observed these ulcerations 81 times in 220 cases of typhoid fever (36.8 per cent.). They appear between the seventh and fourteenth days of the disease, are shallow, and are preceded by a slight discoloration of the mucosa. As a rule they heal in from one to two weeks without leaving any permanent defect. Bacteriologically only the common mouth organisms were found in Devic's cases; but Blume<sup>2</sup> discovered the Eberth bacillus in three out of five cases of ulceration of the palate. The regions at which the ulcers occur are more or less points of compression. As the ulcers are superficial and heal readily, the maintenance of oral cleanliness is sufficient. The frequent presence of the typhoid bacillus apart from ulcers has been shown by Purjesz and Perl.

**Uremia.**—The mouth is frequently affected. There may be an insupportable dryness, or an actual stomatitis which is due to bacterial infection. Instead of dryness of the mouth, there may be salivation without any stomatitis to account for it. Reneon believes that the salivary glands may act vicariously for the kidneys. Uremia may also lead to parotitis. The tongue may be dry and of a maroon-red color. In one case of uremia under the writer's care a tough grayish-white membrane covered lips, gums, cheeks, and pharynx—no other organism but the staphylococcus was demonstrable. Salivation was extraordinarily copious, in part because of inability to swallow.

**Diabetes.**—The tongue in diabetes is large, red, "beefy," and fissured at the margin; the mouth is dry; the teeth are often carious. Pyorrhœa alveolaris is frequent. Diabetes insipidus presents nothing but dryness of the mouth.

**Pernicious Anemia.**—In some cases dental necrosis and ulcerative processes are found in the mouth, which Hunter considers an important factor in the etiology.

**Leukemia.**—The mucous membrane of the mouth may become the seat of lymphoid hyperplasia similar to that found in the lymphatic glands, spleen, and intestines. The infiltrations show a tendency to undergo necrotic change leading to extensive ulceration and pseudomembranous and gangrenous processes. In acute leukemia, gingivitis and ulcerative stomatitis may be among the first signs. As the gums bleed easily, and as there is marked fetor of the breath, the condition may be mistaken for scurvy.

**Scurvy.**—The gums in scurvy are of a purplish color, soft, and bleed easily; the teeth are loosened; there is salivation and intense fetor of the breath. (See Plate IV.) Babes has isolated an organism, *Bacillus gingivitis*, which is found in association with the streptococcus. Oral changes are not always present in scurvy. In the differential diagnosis the possibility of acute leukemia must be kept in mind.

**Locomotor Ataxia.**—Oral conditions found in locomotor ataxia are perforating ulcer (mal perforant buccal) and falling out of the teeth.

<sup>1</sup> Trouillieur, *Gaz. des hôp.*, February 13, 1908, 18, p. 207.

<sup>2</sup> *La Semaine méd.*, January 22, 1908.



The latter is usually entirely painless and may be followed by resorption of the alveolar processes. At times there is anesthesia of the mucous membrane. The buccal changes are probably dependent upon a peripheral neuritis.

**Pregnancy.**—Hyperesthesia, paresthesia, and salivation are common. Sometimes there is inability to chew certain articles of food, which in a case of the writer's extended only to the eating of celery. Pain in the teeth, for the relief of which the teeth are often foolishly sacrificed, is a common symptom of pregnancy. At times there is a true gingivitis.

**Varicella.**—Lesions may occur in the mouth in chicken-pox, but the vesicular stage is rarely observed.

**Variola.**—Lesions of the mouth may appear simultaneously with those upon the skin or later; they are in the form of pustules that soon become macerated and transformed into superficial ulcers. The tongue may be spared.

**Treatment.**—Weak solutions of borax or boric acid, potassium chlorate, or potassium permanganate should be employed. The lesions may be touched with dilute tincture of iodine or the tincture of chloride of iron.

Koplik's spots in measles, the strawberry tongue of scarlet fever, and analogous conditions are described under the respective diseases.

**Pyorrhœa Alveolaris.**—*Synonyms:* Rigg's disease; periostitis alveolaris dentalis; general periodontitis, etc. This is a widespread affection of obscure etiology, occurring usually in persons over thirty years of age. Involving, as it does, a loss of teeth in the best years of life, it ought to interest physicians much more than it has hitherto done. If physicians and dentists would combine in a study of the disease, perhaps the mystery that surrounds it might be lifted.

**Symptoms.**—The gingival mucous membrane is congested and of a deep-red or purplish color. As the gums become detached coincidentally with the destruction of the pericemental membrane and the alveolar osseous tissue, pockets are formed between the root and the alveolus, which are almost constantly filled with inflammatory products and food débris. On pressure against the gums, these pockets may be emptied of their purulent or semipurulent material. The affected teeth, which are tender to the touch, but usually free from caries, gradually become loosened and eventually exfoliated. A general catarrhal condition of the mouth and a characteristic fetor are usually present. The disease may persist for months or years, and while it lasts there is constant swallowing of the purulent exudate and tissue débris, which in time may cause local disturbances in the stomach and general disease. The possible part played by these factors in the production of digestive disorders is often overlooked.

**Diagnosis.**—But little difficulty attends the diagnosis. As a rule, several teeth are affected, chiefly the upper incisors. The swollen, receding gums, and the oozing of pus from pockets beneath the margin are easily discovered signs. Pyorrhœa alveolaris may be an early symptom of diabetes mellitus and of tabes dorsalis, and it may exist for years without being perceived by the patient.

**Treatment.**—Patients should be referred to the dentist for oral treatment. This consists in the removal of all salivary deposits and the scaling and polishing of the surfaces of the teeth. As a stimulating application to the gums after mechanical cleansing, either tincture of iodine or glycerite of tannin may be used. The mouth should be frequently cleansed with a mouth wash, such as the liquor antisepticus diluted or carbolic acid solution (1 per cent.).

Of late, radio-active waters in the form of mouth washes and local radiation with radio-active salts have been recommended. The use of vaccines with proper local treatment has given excellent results in some cases.

### TUBERCULOSIS OF THE MOUTH

This is rarely primary, at least not in the pathological sense; clinically, it may be; at any rate, cases occur in which, aside from the oral or salivary tuberculosis, no other tuberculous lesion is demonstrable. At times, however, repeated careful examination may reveal another focus that constitutes the primary source. In the tonsils an apparent primary localization of tuberculosis has been described.

Tuberculosis in the form of lupus may spread from the face to the mouth. The ordinary form of tuberculosis is usually the result of a direct infection of the mouth with bacteria from the sputum. If there is a hematogenic infection, it has not been demonstrated. It is not likely that this occurs in the tongue, as muscle tissue in general is seldom affected by tuberculosis. Tuberculosis of the *lips* is occasionally seen in tuberculous subjects. It assumes the form of an ulcer, which is not easily distinguished from chancre.

Miliary nodules may appear on the flesh of the *gums*; ulceration may occur along the free edge and extend to the hard palate. The condition has followed tooth extraction in tuberculous subjects. Tuberculosis of the *soft palate* sometimes occurs in persons with pulmonary tuberculosis.

The *tongue* is the commonest seat of oral tuberculosis, the lesion being due to infection from the sputum. Cases are recorded in which the sputum did not seem to be the cause of infection; but in which the latter came from without. The only instance seen by the writer occurred in a street-car conductor, who had the habit of wetting the transfer tickets with his tongue, so as to be better able to separate them with his fingers. S. von Ruck reported 19 cases observed among 5000 patients (0.38 per cent.).

The disease appears in one of several forms, as circumscribed sub-mucous nodules (tuberculomas), which in time ulcerate, as a disseminated process, and rarely in the form of tuberculous fissures or rhagades. The nodules are either single or multiple, and may remain stationary for a long time. Eventually, ulcers form which are shallow, irregular in outline, have undermined edges, and are covered with a grayish-white slough; toward the margin miliary nodules may be seen. Ulcers occurring in association with advanced tuberculosis of the lungs have a greater tendency to spread in extent and depth than those that are apparently

primary. The lymph glands are rarely affected. There is not much pain in the usual chronic non-spreading or slowly spreading ulcers.

**Diagnosis.**—A careful history and discovery of tuberculosis elsewhere aid materially. In differentiating tuberculous and carcinomatous ulcers, the following points are important: tuberculous ulcers may be multiple; the edges are softer and less infiltrated; there is less pain, and less frequent involvement of the lymph glands than in carcinoma; the age of the patient is also of importance.

**Treatment.**—If the pulmonary disease is far advanced, treatment is hardly worth while. In other cases, total excision of the tuberculous area is the best procedure. If not possible, the ulcers may be removed with the thermocautery or sharp spoon. For the dressing of the ulcers, iodoform is best.

### SYPHILIS OF THE MOUTH

In the clinical course of syphilis, lesions of the mouth occupy a prominent place. The *primary sore* is found there in the largest number of cases of so-called extragenital syphilis. The lesion may be only a fissure or a superficial flat erosion, with a pseudomembranous covering. It is usually single, and, even if small, leads to marked glandular enlargement. Its commonest sites are the lips, especially the lower, the tongue, the hard and soft palate, and the tonsils. The danger of infection to others renders it important to make a correct diagnosis early. This is well illustrated by the epidemic of chancre of the lip from kissing reported by Schamberg,<sup>1</sup> in which a man gave chancre of the lip to eight persons. If it is a case of syphilis insontium, the patient is generally unaware of the nature of his ailment. In the diagnosis tuberculous and cancerous ulcers have to be considered. The demonstration of the *Treponema pallidum* in smears from the ulcer facilitates the diagnosis.

**Secondary Lesions.**—The secondary lesions in the mouth are an erythema and the so-called mucous patch. The latter, which is among the most infectious of the syphilitic lesions, is a pearly or milk-white area upon a red inflamed surface. The patches are irregular in outline, and variable in size and number. They are found in all parts of the mouth, most frequently upon the lips, the palatal arches, and the tonsils. At the angles of the mouth they lead to rhagades. They appear about the same time as, or before, the roseola on the skin and may be painful or painless. The diagnosis is not always easy; leukoplakia is to be excluded by its chronicity and by its not occurring on the tonsils and soft palate, as well as by the Wassermann and therapeutic tests.

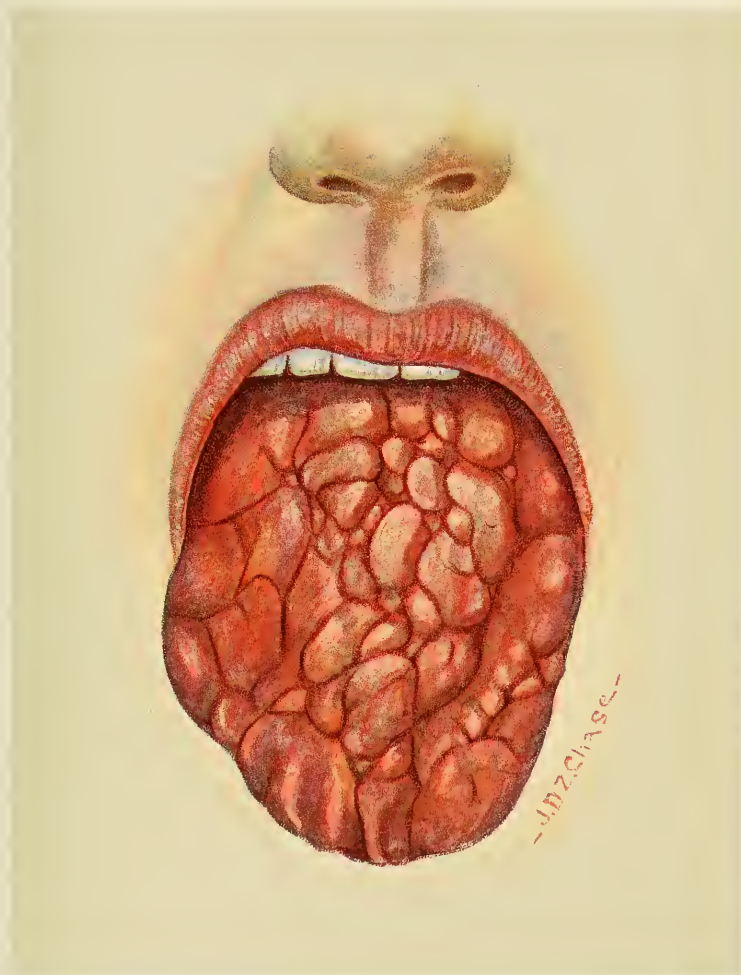
**Treatment.**—The local treatment consists in the use of antiseptic washes in the mouth and direct application of 1 per cent. mercuric chloride solution, of a solution of nitrate of silver (10 to 20 per cent.), or chromic acid solution (5 to 10 per cent.). It is best to use wooden applicators and tongue depressors, and burn them afterwards.

**Tertiary Lesions.**—Tertiary lesions in the mouth are of the nature of gummata and require no special description. Their most frequent

<sup>1</sup> Jour. Amer. Med. Assoc., September 2, 1911.



PLATE V



Syphilitic Lobulation of the Tongue. "Cobble-stone Tongue."





sites are the hard and soft palates; but they may be found in the tongue, lips, and rarely in the cheek. In the palate they usually lead to perforation. The tertiary lesions of the tongue may, according to Fournier, be divided into two types—sclerosing and gummatous glossitis. In the former the infiltration does not break down, but cicatrizes and gives to the tongue a nodular or puckered appearance (*langue lobée, langue rhagadiforme*). The gummatous lesions break down and ulcerate. A tertiary lesion may be mistaken for a primary sore, but, besides being usually deeper, it is not accompanied by marked adenopathy. The history, moreover, is helpful.

**Treatment.**—The treatment consists in the vigorous use of salvarsan and of mercury and potassium iodide.

**Hutchinson's Teeth.**—A crescentic notching of the upper central incisors with a peg shape was described by Jonathan Hutchinson as a sign of inherited syphilis. It is found in the permanent set, and disappears with advancing years through the wearing down of the edges of the teeth. Seldom is the regular crescent found in conditions other than syphilis, and the presence of such teeth always suggests a careful search for additional evidence of congenital lues.

### ACTINOMYCOSIS OF THE MOUTH

Actinomycosis of the mouth is not very common.<sup>1</sup> When it affects the *lips* it produces a tumor-like formation resembling carcinoma. The *cheek* is not often the seat of the disease. In a case of Kaposi's, the trouble began on the inner side of the cheek corresponding to the position of a carious tooth removed a short time before. In the *jaw*, the fungus commonly attacks the periosteum, producing a periostitis alveolaris, especially in the lower jaw. In the *tongue* the disease assumes a tumor-like appearance, the nodules ranging in size from that of a pea to that of a chicken's egg; they are found especially near the tip of the organ.

The cause of actinomycosis is the actinomyces fungus, which is probably conveyed to the mouth clinging to grain. There is no proof of contagion in man from animals. Carious teeth are a predisposing cause by favoring stomatitis, which in turn renders infection with the fungus easier. The cavities in decayed teeth have been suspected to be the breeding places of the actinomyces, but this is not proved.

**Treatment.**—Excision of the diseased area should be done when possible, combined with the use of potassium iodide.

### LEPROSY OF THE MOUTH

This affects the mouth and tongue only secondarily. It appears in the form of nodules, which, in the tongue, may be symmetrically situated on both sides of the raphé; by their coalescence, extensive infiltrating plaques may be formed. Ulceration is rare. The histological lesions are like those of leprosy elsewhere.

<sup>1</sup> *Centralbl. f. die Grenz. der Med. u. Chir.*, 1900, Band 3, iii, p. 561. Also *Deut. Zahnheilk. in Vorträgen*, Heft 30, 1913; *Zeit. f. inn. med.*, June 30, 1913.

### SCLEROMA OF THE MOUTH

This reaches the mouth through the posterior nares, and produces infiltrated areas covered with a somewhat bluish-red mucosa. After a time very hard nodules appear that are not usually spontaneously painful, but somewhat tender on pressure. They scarcely ever suppurate, but may become superficially ulcerated. The infiltration consists of two layers—an upper vascular layer and a lower rich, in cells and traversed by fibrous bands, to which the extreme hardness is due. The similarity to a round-celled sarcoma is quite marked.

### THE TONGUE

The coating of the tongue hardly has the diagnostic value attached to it by the older clinicians. Nevertheless, it gives much information and a study of it should not be neglected. It may depend upon local conditions in the mouth or nasopharynx; upon causes arising from the gastro-intestinal canal; or upon general conditions. A heavy coating is compatible with good health, and the clean tongue is not always a sign that the alimentary canal is performing its functions properly. Some persons have a furred tongue on slight provocation, while others, in severe affections, do not. The tongue is usually heavily coated in persons with restricted movements of the jaw.

An exclusive milk diet nearly always produces a coating of the tongue, probably chiefly because of the suspension of the masticatory movements. In some persons even a single glass of milk will give rise to this condition. A coated tongue is found in mouth breathers, in fevers, and in some forms of dyspepsia. In hyperchlorhydria the tongue is usually dark red, moist, and clean; it is also at times remarkably clean and red in diabetes mellitus. It is pale and heavily coated in anacidity and clean in gallstone disease often when gastric symptoms are marked.

**Anomalies.**—*Aglossia*, a total absence of the tongue, is extremely rare. There is indeed only one indubitable case, that of Jussieu (Rosenthal).<sup>1</sup>

*Microglossia*, smallness of the tongue, is likewise rare.

*Macroglossia*, large tongue, is usually applied to enlargements of the tongue not due to acute inflammation, and is of four varieties: (a) Lymphatic (lymphangioma); (b) cavernous (hemangioma); (c) muscular or parenchymatous, the rarest, of which Helbing<sup>2</sup> reports a case; (d) neuromatous macroglossia, of which cases have been described by Abbott and Shattuck<sup>3</sup> and Wagner.<sup>4</sup> A chronic enlargement, due to syphilis, might be added to the foregoing. Macroglossia is generally bilateral, but may be unilateral, as in the case of Little,<sup>5</sup> in which it was

<sup>1</sup> *Die Zunge*, 1903, p. 17.

<sup>2</sup> *Jahrb. f. Kinderh.*, 1895 to 1896, xli, p. 442.

<sup>3</sup> *Annals of Surgery*, 37, 1903.

<sup>4</sup> Cited in *Ztschr. f. d. gesam. Med. u. i. Grenzgeb.*, May 26, 1913.

<sup>5</sup> *British Journal of Dermatology*, 1906, xviii, p. 181.

probably due to congenital syphilis; and in that of Maas, in which it was associated with congenital hypertrophy of one-half of the body. The chief causes of macroglossia are cretinism and syphilis; the former producing especially the lymphangiomatous form, which may be associated with *macrocheilia*, large lip. In the cases due to cretinism, thyroid extract might be useful. In a case reported by Comroe<sup>1</sup> a cure was brought about the excision of a V-shaped piece.

*Doubling of the tongue*, excessively long tongue, and *bifid* tongue have been described, but are unimportant.

*Congenital deformities of the frenum* are supposed to be common, and to the so-called tongue-tie the laity ascribe delayed talking and difficulty in sucking. Cutting of the frenum is, however, very rarely necessary, although Makuen<sup>2</sup> has reported a case of rapid speech development in an adult following the operation for tongue-tie. In a case of the writer's, a trained nurse, the tongue-tie prevented protrusion of the organ but did not materially interfere with speech.

*Tongue swallowing* may occur if the frenum is too long. The tongue may roll back and so press against the posterior wall of the pharynx that the entrance to the larynx is occluded and suffocation results.

*Tongue sucking* is especially common in Mongolian idiots. It leads to marked fissuring of the tongue and to enlargement of the papillæ.

*Scrotal tongue* (langue scrotale) is a term much used by the French to describe a fissured tongue resembling the scrotum in its roughness. It is difficult to find an explanation for it, although sometimes there is a history of gastro-intestinal disorders. Some of the patients in early life were arthritic subjects. The condition may run in families.

**Black Tongue.**—*Synonyms:* Lingua nigra; nigrities linguæ; hyperkeratosis of the tongue; melanotrichia of the tongue; melanoglossia; German—Haarzunge. This is a condition in which a brownish or black patch appears on the posterior portion of the tongue, in the neighborhood of the circumvallate papillæ. It is either smooth or covered with densely intertwined hair-like processes varying in length up to 1 cm. The hairs are elongated filiform papillæ that have become pigmented and cornified. Some hold that the black discoloration is due to a mould; but Blau found no mould in four cases. The causes of black tongue seem to be various. Heidingsfeld<sup>3</sup> thinks that the true or permanent cases have a congenital origin and are due to some anomaly of development. The spurious cases of black tongue are caused by local or general irritating or infectious agencies, such as tobacco, syphilis, antiseptics, etc. A parasitic origin has not been established. It has been found in syphilis, diabetes, neuralgia, etc. It may come and go without treatment, and this suggests that it depends upon changes in the salivary secretion. There are usually no subjective symptoms.

**Varicose Veins of the Tongue.**—Dilatation of the ranine veins on the under surface of the tongue is not uncommon; but the veins on the dorsum may also become varicose, especially those running from the base forward to the circumvallate papillæ. The causes are local.

<sup>1</sup> *Cleveland Med. Jour.*, September, 1911.      <sup>2</sup> *New York Med. Jour.*, 1895, p. 20.

<sup>3</sup> *Jour. Amer. Med. Assoc.*, December 17, 1910.



**Hemorrhage from the Tongue.**—Bleeding tongue, glossorrhagia. This is most often traumatic, but may occur in purpura and other hemorrhagic conditions, and in hysteria, of which the writer has seen a striking example. (See Plate VI.)

**Paralysis of the Tongue.**—Glossoplegia. This may be due to central or peripheral lesions of the nervous system, and is either unilateral or bilateral. Unilateral glossoplegia may be caused by disturbance of one of the hypoglossal nerves; it is also present in the majority of cases of cerebral hemiplegia. The tongue is deflected toward the paralyzed side. The chief cause of bilateral glossoplegia is progressive muscular atrophy.

**Spasm of the Tongue.**—The tongue participates in the general muscular commotion in epilepsy, chorea, etc. Spasm limited to the tongue, a sort of tic, has been described; spasm of the facial and masticatory muscles may be associated with it. Some cases of spasm are hysterical; in some no definite cause is discoverable.

**Paralysis of the Soft Palate.**—This, like glossoplegia, may be unilateral or bilateral. In the unilateral form the palate on the affected side hangs lower than on the normal side. In bilateral palsy the entire palate droops and is motionless during speaking and breathing; speech and swallowing are disturbed, and food regurgitates through the nose. The most important causes are neuritis following infectious diseases, especially diphtheria; bulbar palsy, tumors at the base of the brain in the posterior fossa; aneurism of the vertebral artery; and tabes dorsalis.

**Glossitis.**—Acute inflammation may be due to biting of the organ during an epileptic convulsion, biting by insects, burns, or to the irritation of a rough, carious tooth. An acute glossitis occurs in smallpox, erysipelas, scarlet fever, and typhoid fever, and usually accompanies severe forms. Tobacco may also cause glossitis and is responsible for the so-called smoker's patch.

**Symptoms.**—The affected side of the tongue swells and at the point of injury becomes covered with a grayish-white membranous deposit. The swelling may be so great that the tongue hangs out of the mouth. Pain and discomfort are severe and mastication may be impossible. The saliva is increased in amount and is sticky. The condition usually terminates in resolution; but in about one-third of the cases, according to A. B. Bennett,<sup>1</sup> suppuration ensues. When unilateral in the beginning (hemiglossitis), it rarely spreads to the other side.

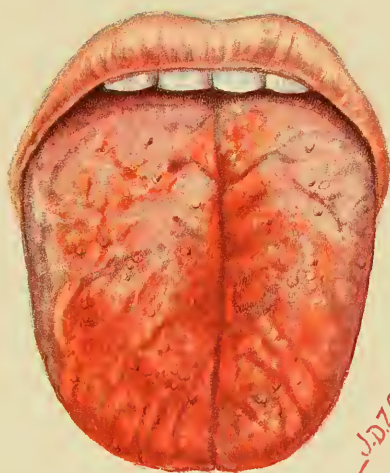
**Treatment.**—Antiseptic mouth washes are indicated. In severe cases, and when abscesses form, a long, deep incision must be made into the substance of the organ.

**Papillitis Lingualis; Linguopapillitis.**—This is a painful condition of the tongue, which reveals nothing to the naked eye, but the magnifying lens shows small, ulcerating points hidden in the folds of the mucosa about the fungiform papillae of the tip and margin of the tongue.

**Treatment.**—The painful points should be touched with the galvano-cautery, aided by a lens.

<sup>1</sup> *Albany Med. Ann.*, 1906, v, p. 667.

PLATE VI



-J.D.Z. Chase-

Bleeding Tongue in Hysteria.



**Ulcer of the Frenum.**—Ulcer is most common in children suffering from whooping-cough, and is due to the forcible protrusion of the tongue and impact of the frenum against the teeth during the paroxysms.

**Glossitis Papillosa Acuta; Glossitis Papillaris.**—This is an inflammation limited to the circumvallate papillæ, and is characterized by slight difficulty in swallowing, burning, and sticking sensations in the throat, and an irritative cough. An acute form has been described by Michelson.<sup>1</sup> Stetter,<sup>2</sup> under the name of glossitis papillaris, reports four cases with histological studies. Tuberculosis may produce conditions very similar to the ones described.

**Wandering Rash of the Tongue.**—*Synonyms:* Geographical tongue; exfoliatio areata linguæ; état lichenoidé; annulus migrans; Zungenfratt; état tigré; glossitis exfoliatricans marginata; desquamation en aires. This interesting condition of the tongue is characterized by circinate, crescentic, or circular patches in which the epithelium is desquamated. The patches may be multiple or single, they may affect the dorsum or the margin of the tongue and are bordered by a slightly elevated, whitish ring which is sometimes double-contoured. When the patches are multiple and affect a large part of the tongue the fantastic shapes give a remarkable appearance well described in the name geographical tongue. The patches may come and go suddenly; their shape and size may alter rapidly. Contiguous patches may fuse. In some cases a single patch may remain for a long time unchanged.

**Etiology.**—The cause is not definitely known. Gastro-intestinal disorders and heredity are possible factors. A single patch may be due to a sharp tooth. Syphilis is not responsible for the condition.

Histological examination shows a superficial desquamation of the epithelium, the latter being replaced by a coagulated exudate containing leukocytes and degenerated epithelial cells. The cells of the deeper layers of the mucosa are in a state of cloudy swelling. Some authors have found the changes most marked in the lower strata of the mucosa.

**Symptoms.**—There are usually no subjective symptoms except a little burning or sensitiveness. The affected area looks paler and smoother than the surrounding parts. The lymphatic glands may be enlarged; in women the condition is apt to be worse at the menstrual periods. Some patients, fearing cancer, become hypochondriacal.

**Treatment.**—It usually subsides without treatment. Attention should be given to the gastro-intestinal canal. The patient's mind should be put at rest as regards cancer. A mouth-wash of sodium hyposulphite and glycerin, of each 10 parts, and water 180 parts, may be used.

**Moeller's Glossitis; Glossodynia Exfoliativa; Chronic Superficial Glossitis.**—This is a very painful affection of the tongue, characterized by bright-red lines or patches at the margin and tip. The pain, which is the principal symptom, is out of proportion to the local lesion, and is much increased by chewing and speaking. The disease chiefly affects women, especially those who are weak and decrepit. The cause is unknown. The only instance seen by the writer was in a woman with

<sup>1</sup> *Berl. klin. Woch.*, 1890, p. 1094.

<sup>2</sup> *Arch. f. klin. Chir.*, 1898, lvi, p. 324.



pernicious anemia. Local treatment was of no avail; the x-ray and applications of nitrate of silver were tried without effect. With an improvement in the blood the condition subsided, but recurred; the patient eventually died of anemia.

**Glossodynia.**—Pain of the tongue, without gross lesion to account for it, is not uncommon; usually the pain is referred to the anterior third of the organ or along the margin of the tip. It is often difficult to ascertain the cause; but in a search for it the classification of Chaveau<sup>1</sup> may prove helpful. He names the following varieties:

1. Glossodynia secondary to trigeminal neuralgia, especially of the inferior dental branch of the trigeminal.

2. Glossodynia of the insane, usually starting as a local paresthesia.

3. Glossodynia of tabes, corresponding to the crises in other organs.

4. Glossodynia of hysteria.

5. "Rheumatism" of the lingual muscle or rheumatic glossodynia.

6. Glossodynia attributable to local causes. These may be extrinsic or intrinsic. Among the extrinsic causes are (a) dental affections and artificial teeth (causing papillary hypertrophies and other lesser lesions); (b) granular pharyngitis and hypertrophy of the posterior pillars, and of the lingual tonsil, etc. Among intrinsic causes are mentioned (a) lingual varices; (b) chronic glossitis from tobacco, alcohol, spices, iodine, lead, gout, etc., and (c) papillary hypertrophy.

**Leukoplakia.**—*Synonyms:* Leukoplasia; psoriasis linguæ; tylosis linguæ; ichthyosis buccalis; keratosis buccalis; smoker's patch. This is a chronic disease of the mucous membrane of the tongue, rarely of the lips, cheek, palate, and gums, characterized by thick, elevated, indurated, whitish patches having either a fissured or more rarely a smooth appearance.

**Etiology.**—There is a connection between syphilis and leukoplakia, but that the former is the cause cannot be maintained, in view of the investigations of Erb<sup>2</sup> and Neisser.<sup>3</sup> Nevertheless, the frequency of a history of syphilis, in 65 per cent. of the cases of leukoplakia, according to Schoengarth,<sup>4</sup> and in Pulvermacher's<sup>5</sup> 54 cases, seem to justify the contention that leukoplakia is a parasymphilitic lesion. Ivy<sup>6</sup> obtained a negative Wassermann in 2 out of 3 typical cases. This was also true of one of the writer's cases that eventuated in carcinoma. Smoking is also an important factor, and explains in a measure the predominance of the disease in the male sex. Of Pulvermacher's 54 patients, only 1 was a woman. The use of spices, condiments, and alcoholic beverages must be mentioned among the possible causes, likewise irritation by carious teeth and badly-fitting dental devices. As leukoplakia has been found associated with diseases of the skin characterized by scaling and keratosis, it may be looked upon as an expression of a general tendency to hyperkeratosis, to which the mouth is excited by frequently repeated or

<sup>1</sup> *Arch. gén. de Méd.*, 1900, ann. 77, n. s., iii, p. 66.

<sup>2</sup> *Munch. med. Woch.*, 1892, Nr. 42.

<sup>3</sup> Quoted by Mikulicz and Kummel, *Die Krankheiten des Mundes*.

<sup>4</sup> *Ueber Leukoplakia lingualis et buccalis*; *Diss. Breslau*, 1896

<sup>5</sup> *Wien. klin. Woch.*, 1906, xiii, p. 963.

<sup>6</sup> *New York Med. Jour.*, April 13, 1912.

long-continued irritation of various kinds. The most common dermal association is psoriasis.

The disease is most common in the male sex and in adult life, although Hartzell reports a case of extensive leukoplakia associated with keratosis of the skin in a young girl aged eleven years. The disease progressed steadily until at the age of twenty-six there was carcinoma of the tongue.

**Pathology.**—The principal feature is a hyperkeratosis of the mucous membrane. The epithelium, especially the corneous layer, is greatly thickened. The subcorneous stratum contains many cells filled with eleidin droplets and granules. Mitotic figures are abundant in the deeper layers of the rete mucosum; while the elongated papillary processes are extensively infiltrated with leukocytes.

**Relation to Epithelioma.**—The transformation of leukoplakia into cancer is indubitable. This is not a complication or an accident, but a distinct evolutionary development, the causes of which reside in the histogenesis of leukoplakia. It occurs in about 20 per cent. of the cases.

**Symptoms.**—In the early stages leukoplakia appears in the form of deep-red erythematous patches, which after a short time assume a bluish-white color, looking as if the mucous membrane had been painted over with a strong solution of silver nitrate. Gradually the patches become thicker and larger, and, in the case of the tongue, may cover the mucosa so completely that the papillæ are no longer visible. The parts affected are in the order of frequency: tongue, lips, cheek, gums, and palate. The pharynx and the base of the tongue posterior to the circumvallate papillæ are rarely involved. The patches may be smooth, more often they are fissured. To the touch they have a tough, leathery feel. The superficial layer can at times be picked off easily without much bleeding being produced; regeneration quickly takes place.

The subjective symptoms are slight, unless the fissures are deep and raw, in which case there may be pain on chewing. The patient who is aware of his leukoplakia is apt to become hypochondriacal, fearing either cancer or that syphilis is returning under a new form.

**Treatment.**—This avails but little, and it is doubtful whether it is possible to prevent by any form of application the development of carcinoma. Cleanliness of the mouth, cessation of smoking, abstention from irritant spices, and the removal of sharp-edged teeth are important. Antiseptic treatment and strong caustics more often do harm than good. A 10 per cent. solution of tincture of iodine has been recommended, and Hartzell advises applications of salicylic acid (1 to 100 or 150). The x-ray cautiously employed has been of some value in the hands of Hartzell and Schamberg (personal communication). Bockhart insists that leukoplakia cannot be cured unless the patient stops smoking. In five cases he had success with the following local treatment: the diseased areas were rubbed once a day or once in two days with balsam of Peru; in addition the mouth was rinsed from six to twelve times a day with from  $\frac{1}{2}$  to 3 per cent. salt solution. He considers the saline washing more important than the application of the balsam. Antisyphilitic treatment is not only useless but often harmful. Local astringents, such as myrrh, are injurious.

**Smooth Atrophy of the Tongue.**—This is an atrophy of the epithelial covering and of the large sebaceous glands at the base of the tongue, which is found more often in acquired syphilis than in any other condition, and has been considered a pathognomonic sign of this disease. Goldschmidt<sup>1</sup> found it in 17 per cent. of 140 cases of secondary, and in 47 among 60 cases of tertiary syphilis. But as it is also found in non-syphilitic subjects, it cannot have the diagnostic value ascribed to it. L. S. Milne<sup>2</sup> found it 39 times in 505 autopsies (25 male, 14 female). Among 36 syphilitic cases, it occurred 14 times, a sufficiently large proportion to make the relation significant. It was also found a few times in tuberculosis. In examining for it, the finger or the mirror may be used. With the former, the unnatural smoothness of the base of the tongue is perhaps more readily detected.

**Riga's Disease.**—*Synonym:* Produzione sottolinguale. This is a benign tumor-like excrescence on the lingual frenum of infants. It is most common in Italy, whence nearly all the observations and studies have come. Good accounts, with bibliographies, are found in the articles of Ernst Deutsch<sup>3</sup> and E. Audard.<sup>4</sup> The cause is in dispute, but in some cases it is of mechanical origin (decubital), due to irritation by the lower incisor teeth. Histologically, it is a papillomatous growth.

**Symptoms.**—The disease appears between the ages of three and eighteen months and is equally common in both sexes. It is probably not contagious; some Italian writers, however, consider it so. It lasts from two weeks to two months; although some cases are on record that persisted for from eighteen to twenty months. It must be distinguished from the ulcer of whooping-cough, chicken-pox, syphilitic ulceration, herpes, and impetigo.

**Treatment.**—If a cause is discoverable, it should be removed. If there is irritation by teeth, they should be extracted. In persistent cases, caustics, silver nitrate or tincture of iodine, may be applied, or the growth may be excised.

**Tumors.**—*Fibroma*, usually of the hard variety, is found on the surface or in the substance of the organ. *Sarcoma* is a comparatively rare tumor, generally spindle-celled, and occurs in the substance of the tongue.

**Thyroid Tumors.**—A small tumor is sometimes found at the base of the tongue in the region of the foramen cæcum, which histologically is made up of tissue closely resembling that of the thyroid gland and the origin of which is to be traced to the remains of the thyroglossal duct. Glas<sup>5</sup> reported a case of adenomyoma occurring in the same region as the thyroid tumor, traced to the remains of the ductus lingualis.

*Carcinoma* is the most frequent tumor found in the tongue. It is commoner in the male sex (66 to 3 in the statistics of Meller), and extremely malignant. Patients not operated on usually die in less than a year after the appearance of the first symptoms.

*Amyloid tumor* is rare; an example is recorded by Gross.<sup>6</sup>

<sup>1</sup> *Berl. klin. Woch.*, 1899, Nr. 43.    <sup>2</sup> *Jour. Amer. Med. Assoc.*, September 23, 1911.

<sup>3</sup> *Arch. f. Kinderh.*, 1905, xl, p. 168.

<sup>4</sup> *Rev. mensuelle des mal. de l'enfance*, 1902, xx, p. 49.

<sup>5</sup> *Berl. klin. Woch.*, 1905, 18, p. 746.    <sup>6</sup> *Deut. Zeit. f. Chir.*, 1906, 84, p. 462.



## THE SALIVARY GLANDS

The normal saliva is composed of the secretions of the salivary glands—the parotid, submaxillary, and sublingual—and of the mucous glands of the mouth. It is a watery, opalescent, slightly stringy fluid, of a feebly alkaline reaction, and has a specific gravity of from 1002 to 1008. Its principal organic constituents are mucin—a diastatic ferment—ptyalin, oxydases, and slight traces of protein. Urea, according to some authorities, is also present. Among the inorganic constituents are potassium and sodium chloride, potassium sulphate, sodium carbonate, calcium carbonate and phosphate, potassium sulphocyanide, and carbon dioxide. The total solids amount to from 5 to 10 parts per 1000. The freezing point is  $0.20^{\circ}$  C. Apart from the fact that the protein is a glycoprotein, nothing definite is known of its nature. The potassium sulphocyanide content varies considerably. In smokers it is said to be greater (0.2 per 1000) than in non-smokers (0.03 or 0.04 per 1000).

The *secretion* of the saliva is under the control of two sets of nerves: one from the brain, the other from the sympathetic system. In the case of the submaxillary gland, the cerebral impulses are conveyed by fibres of the facial nerve running in the chorda tympani. Studies on animals have shown decided differences in the saliva following separate stimulation of these two types of nerve fibres. The *sympathetic saliva* is scantier, thicker, and richer in solids, particularly in mucin, than the *chorda saliva*. A third variety of saliva is the so-called *paralytic saliva*, which follows poisoning with curare or section of the gland nerves. The normal daily quantity of saliva varies from 1400 to 1500 cc.

The reaction, usually alkaline, is subject to variations. It may be acid or neutral even in health; in diabetes, fevers, and dyspepsia it is often acid. In making tests, the possibility of acid mouth washes being used should not be overlooked. The relative proportion of organic as well as inorganic constituent changes in response to variations in the stimulus. Von Zebrowski has shown that the quality of the excitant and intensity of its action, as well as the locality and manner of its application, are of importance. The secretion of saliva is stimulated more by those substances that require longer chewing. In unilateral mastication, the gland on the active side is especially stimulated; the opposite gland also secretes, but more slowly, and the saliva contains a somewhat larger amount of organic substances.

Stern and Lederer,<sup>1</sup> in a study of the saliva in 158 cases of diabetes mellitus, found the quantity increased in 8, diminished in 89, normal in 63. The reaction was acid in 47, alkaline in 92, neutral in 8. Glucose was found in 85. The diastatic quality was unchanged in 90 per cent. When the sugar disappeared from the urine it also disappeared from the saliva. In acute gastritis an acid secretion was found in 8 out of 20 cases, being caused in 2 by lactic acid and in 2 by acetic acid. In hyperchlorhydria an increase of secretion was found in 27 out of 182 cases; the

<sup>1</sup> *Jour. Amer. Med. Assoc.*, 1904, xliii, p. 1765.



reaction was acid in 71, alkaline in 41, neutral in 5, amphoteric in 65. The acid reaction was due to lactic acid in 12, to acetic acid in 12, to lactic and acetic acids in 9, to hydrochloric acid in 6. In pyloric stenosis the reaction was acid in 5, alkaline in 8; in hypochlorhydria the reaction was acid in 2, alkaline in 15, and amphoteric in 6. Urea is increased in severe nephritis and in uremia.

1. **Increase of salivary secretion** (hyperptyalism, ptyalism, salivation, sialorrhœa, sialosis) is often apparent rather than real, the saliva, normal in amount, not being swallowed. This is the case in paralysis of the muscles of deglutition, or of those of the lips and tongue; in quinsy and other forms of tonsillitis, and in severe types of pharyngitis, when swallowing is painful. True hyperptyalism is a condition in which more than the normal amount of saliva is secreted. Its causes are various:

(a) *Local*.—The different forms of stomatitis; dentition; and chorea, by reason of the active masticatory movements.

(b) *Reflex*.—Hyperchlorhydria; gastric ulcer; nausea; pregnancy; trigeminal neuralgia; helminthiasis; pancreatic calculus; pain from various sources. The most profuse salivation ever seen by the writer occurred in a man who had been operated upon for hernia. No tangible cause aside from the operation could be found. In a woman, suspected of being a morphine habituë, there was a constant flow of a sticky saliva while she was under surveillance and could not obtain the drug. The salivation subsided immediately after a small morphine injection.

(c) *Direct nerve stimulation*, either central or peripheral; migraine; bulbar palsy; uremia; certain poisons, as, for example, mercury. The salivation in the last-named is only in part due to stomatitis, for it often precedes inflammatory changes in the mouth. Certain drugs, such as pilocarpine, act through direct stimulation of the nervous system. Hysterical and neurotic salivation, which in some cases depend on direct nervous influences may also be reflex.

*Salivation in Children*.—Salivation is normal in infants; it is increased by dentition, but is not dependent upon it. Salivation is present in all forms of stomatitis, and, without any local changes in the mouth, in cretinism and idiocy. Jordan reported two cases of "idiopathic salivation" in children. The dribbling began during dentition and continued, without any apparent cause, after the process had stopped.

2. **Diminution of secretion** (hypoptyalism, aptyalism, absence of secretion) occurs in fevers, especially in pneumonia, typhoid fever, and septic fevers; after the use of atropine; in fright and excitement (the rice ordeal); in loss of fluid through diarrhœa or the elimination of dropsical effusion; in cirrhosis of the liver when ascites is forming, and in atrophy of the salivary glands. The writer has also noticed an annoying dryness in arteriosclerosis with great hypertension and polyuria, with and without thirst.

**Xerostomia**.—Under the name of xerostomia, or dry mouth, Jonathan Hutchinson<sup>1</sup> described a condition of distressing dryness due to suppression of the salivary secretion. It is most common in women (32

<sup>1</sup> *Clin. Soc. Trans.*, 1888, xxi, p. 180.

women to 4 men, in Hall's table),<sup>1</sup> and usually resists treatment. In a case of the writer's, a woman aged thirty-eight years, the dryness had lasted two years, and was so great that the patient had to rise two or three times a night to wet her mouth. The urine amounted to two liters a day, had a low specific gravity, 1008, and was free from albumin and sugar. There were also darting pains in the tongue (glossodynia), and her speech was somewhat disturbed. In other cases reported, mastication and swallowing were affected.

The tongue and mouth are dry, red, and glazed, and there seems to be suppression not only of the salivary secretion, but also of that of the buccal glands. In 8 cases of 39 (Hall) the parotids were enlarged. The disease began suddenly in 6; in 6 it followed mental shock, and in 4 influenza or other slight febrile affections.

**Etiology.**—The condition is in the majority of cases best explained on the basis of a disturbance of the nerve centres controlling the secretion of the salivary and buccal glands. In some instances it may be due to a primary affection of the salivary glands, since it is present in the so-called Mikulicz's disease. Zagari<sup>2</sup> found atrophy of the parotid and submaxillary glands (histologically determined) in a case of xerostomia in a woman aged fifty years, who had died of a gradually increasing emaciation and marasmus.

**Treatment.**—The condition has generally proved rebellious to treatment. The galvanic current is worth a trial, and pilocarpine in small doses may also be employed.

**Acute Inflammation.**—Acute inflammation of the parotid gland—parotitis—appears in two forms: the epidemic parotitis or mumps, and the so-called secondary parotitis, which is found associated with typhoid and septic fevers, pneumonia, dysentery, pyelitis, smallpox, measles, scarlet fever, and is also seen at times after abdominal operations, especially oöphorectomy. As far as the writer's observation goes, it is most common with diseases situated below the diaphragm. In obscure febrile cases the appearance of a parotitis should lead the physician to consider carefully the possibility of typhoid fever, abscess in the pelvis of the kidney, or a perinephritic abscess. The condition has also been called splanchnic parotitis. A parotitis occurring in the course of hemiplegia was described by Gilbert and Villaret.<sup>3</sup> In both cases observed by them the parotid on the paralyzed side was affected.

**Parotitis Due to Drugs.**—The writer has seen an acute enlargement of the parotid gland following the administration of potassium iodide; it may also occur as a complication of lead poisoning.

**Chronic Inflammation.**—Chronic inflammation usually depends on retention of salivary secretion, and is most common in the parotid. The gland is enlarged and hard, and may resemble a malignant tumor. The disease is attributable to an infection propagated from the buccal cavity, and is often associated with the presence of stones in the ducts or the

<sup>1</sup> *Quarterly Medical Journal*, 1898-99, vii, p. 26.

<sup>2</sup> *Il Policlinico*, 1907, xiv, Medical Section.

<sup>3</sup> *Sem. méd.*, 1906, p. 104.

glands themselves. The size of the gland varies according to the degree of obstruction and retention.

**Sialodochitis Fibrinosa.**—Under this name Emden<sup>1</sup> reports the following case: A woman, aged fifty-four years, suffered at first in long intervals, later, regularly every eight days, from bilateral swelling of the submaxillary and sublingual glands. The attack began with burning pain in the tip of the tongue, was unaccompanied by fever, and produced a firm, dense infiltration of the glands. The whole process subsided after three days, with expulsion from the salivary caruncles of fibrinous plugs, and with profuse salivation. The plugs measured several centimeters in length and branched dichotomously. Emden compares the condition to fibrinous bronchitis, and, while not denying the possibility of a secretory neurosis, attributes it to inflammatory changes in the salivary ducts. Analogous cases have been reported by Naegeli-Akerblom,<sup>2</sup> and by Viaud,<sup>3</sup> who coined the term "whartonitis."

**Periodic Swelling of the Salivary Glands.**—Certain persons are subject to recurrent attacks of swelling of one or both parotid glands which subsides quickly in a day or two. It is probably due to temporary obstruction of Stenson's duct and seems to follow exposure to cold, but may have other causes. Cases of this type have been reported by Lange<sup>4</sup> and by Lüders.<sup>5</sup>

**Tuberculosis.**—The salivary glands are not often attacked by tuberculosis, a comparative immunity they share with the pancreas. Even experimentally, infection of the glands is not easily accomplished unless their nutrition is first disturbed by trauma. In man tubercle bacilli may reach the glands through the blood, the lymphatics, the excretory duct, or by direct extension from neighboring parts. It is still a question, however, whether in the so-called primary form of tuberculosis the disease is not located in a lymph gland occasionally found embedded in the parotid, from which the disease extends to the parenchyma proper. Mintz<sup>6</sup> collected 8 cases of so-called primary tuberculosis affecting the parotid; and O'Zoux<sup>7</sup> found 4 of the submaxillary. Legueu and Marien, finding in their cases chiefly parenchymatous lesions, concluded that the infection had been propagated along the duct. Bockhorn,<sup>8</sup> Mintz,<sup>9</sup> and Lecéne<sup>10</sup> believe in lymphatic transmission, the principal lesions in their cases having been found in the intra-acinous connective tissue. The infection, whether it travels by the one route or by the other, usually occurs through carious teeth or ulcerated gums about such teeth. Tuberculosis of the salivary glands is of slow development, and is generally mistaken for the so-called mixed tumor.

<sup>1</sup> *Sitzungsbericht des aerztl. Vereins in Hamburg*, 1897.

<sup>2</sup> *Monats. f. Ohrenheilk.*, 1895, Band xxix, S. 80.

<sup>3</sup> *Thèse de Paris*, 1894.

<sup>4</sup> *Deut. med. Woch.*, 1912, No. 6.

<sup>5</sup> *Ibid.*, No. 12.

<sup>6</sup> *Deut. Ziet. f. Chir.*, 1901, lxi, p. 290.

<sup>7</sup> *Arch. clin. de Bordeaux*, 1897, vi, p. 28.

<sup>8</sup> *Arch. f. klin. Chir.*, 1898, lvi, p. 189.

<sup>9</sup> *Deut. Zeit. f. Chir.*, 1901, lxi, p. 290.

<sup>10</sup> *Rev. de Chir.*, 1901, xxiii, p. 524.



**Syphilis.**—This is rare, and has hitherto been found principally in the sublingual gland, occasionally in the parotid gland (Crile). It is usually of the tertiary form, and in the differential diagnosis, which may be difficult, the history, the Wassermann test, and the therapeutic test give the most assistance.

**Tartar or Salivary Calculus.**—Tartar is a laminated deposit upon the teeth, varying in color and density. The common sites are the lingual surfaces of the lower incisors and canines, and the buccal surfaces of the upper molars. Two varieties are described, the soft and the hard; the former being rapidly deposited, buff colored and abundant; while the latter is slowly deposited, dark, and firmly adherent to the tooth surface. Calcium carbonate and calcium phosphate make up the bulk of salivary calculi. Traces of iron phosphate and silica are sometimes present. The deposit of tartar leads to more or less absorption of the alveolar process and to chronic gingivitis.

**Treatment.**—This consists in the removal of the tartar by a dentist. Careful brushing of the teeth is the only means of retarding the accumulation of salivary calculus.

**Stones Proper; Salivary Calculi.**—Stones may form in the ducts, rarely in the glands themselves, the most frequent site being Wharton's duct, at a point from 10 to 20 mm. from the salivary caruncle. They seldom exceed the size of a pea, and are composed chiefly of calcium phosphate or calcium carbonate, which constitutes from 62 to 95 per cent. of the stone. They are usually single, but in the case of Brin there were four in one duct. Duct stones are cylindrical and smooth; gland stones usually round or irregular. The writer has seen three cases of salivary calculus, all in women.

**Etiology.**—Stones formed in the ducts may have a foreign body, such as grains, seeds, bits of food or tartar as a nucleus, but it is probable that the impetus to stone formation is given by bacterial infection. Inflammatory changes in the glands, by bringing about a change in the consistency of the saliva, may lead to stone formation. In several cases there was long-continued irritation of the mouth by a pipe.

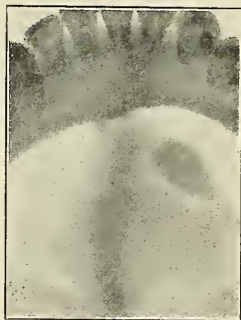
**Symptoms.**—Stones located in the glands do not, as a rule, give rise to marked symptoms, although the gland may be enlarged, firm, and tender. The characteristic feature is an intermittent pain along the floor of the mouth, the so-called salivary colic, which usually comes on during eating and persists for from one to several hours. It is associated with a similarly intermittent tumefaction of the gland and a distension of the proximal part of the obstructed duct. At times there is a purulent discharge (pyorrhœa salivaris) which may be exceedingly offensive. The stone can generally be detected by sounding, by digital palpation, or by means of the x-ray.

Salivary calculi situated on the floor of the mouth may simulate ranula, from which they may be distinguished by noting that in calculus the flow of the saliva is stopped and that a probe cannot be passed along the duct, while careful digital exploration or the x-ray may reveal the concretion. Malignant disease, actinomycosis, and tuberculosis must also be borne in mind.



**Treatment.**—The treatment consists in the removal of the stone. Sometimes this can be accomplished by pressure and a probe. The writer succeeded by these means in a case in which the concrement was located near the outlet of Stenson's duct. When the stone is deep-seated, operation is necessary. In rare instances the stone becomes quiescent and demands no special treatment.

FIG. 1



x-ray picture of a salivary calculus.

**Tumors.**—The most interesting as well as the most important new-growth is the so-called *mixed tumor*, which has puzzled pathologists for many years. Clinically, it is a slowly growing, movable, smooth or nodular tumor, usually painless, disfiguring, and often reaching an enormous size. It is more common in the parotid than in any other of the salivary glands, the distribution, according to Boehme, being as follows: 74.1 per cent. of all cases affect the parotid, 7.7 per cent. the submaxillary, and 1.1 per cent. the sublingual. The skin is rarely adherent. The tumors have a capsule composed of fibrous connective tissue; sometimes nodules of unchanged or inflamed salivary gland tissue are included within the capsule. From the capsule septa extend inward and subdivide the tumor into lobules. The color varies from reddish to yellowish gray. According to the amount of mucoid or hyaline degeneration, the surface is opaque, glistening, or gelatinous; at times cystic spaces are present. If the tumor is malignant, it bursts through its capsule and infiltrates the neighboring tissues; it may cause metastasis in the regional lymph glands, but transference to distant organs is rare. The soft tumors are more malignant than the hard ones, though local recurrence is more common in the cartilaginous forms.

Microscopic studies reveal a very complicated structure, suggesting in some cases carcinoma, and in others sarcoma. Mucoid and fatty tissue and cartilage may still further obscure the picture. In a goodly proportion of cases, in 14 of 26 studied by Ehrich, squamous epithelium is present and may show characteristic horny changes. The cells which constitute the tumor parenchyma proper are arranged in larger or smaller masses resembling gland acini, or in tubules, the lumen of which

is lined with cubical or cylindrical cells. It is the origin of these cells that has given rise to most dispute. Some authorities hold that the cells spring from the endothelium of the lymph spaces or perivascular lymph sheaths, and that the tumors must be classed with the endotheliomas and peritheliomas. Küttner,<sup>1</sup> in a study of 97 tumors of the submaxillary gland collected from the literature, found 64 to be endotheliomas, 6 sarcomas, 3 adenomas (?), 5 carcinomas, and 19 of doubtful nature. The endotheliomas may be benign or may resemble sarcoma and carcinoma in the malignancy of their course. Those not having cartilage show a greater tendency to malignancy than the enchondromas.

There are many writers, however, who contend that not only morphologically, but also histogenetically, the tumor cells are epithelial. Given certain conditions of growth, endothelium can easily assume the shapes of epithelial cells. Those tumors in which masses of squamous epithelial tissue are found may, as many have shown, take their origin from remains of the branchial arches. Guleke<sup>2</sup> believes that some of the parotid tumors are teratomas and arise from germinal displacements of the original salivary gland "Anlage;" this latter contributing the cellular elements of the tumor, while the myxomatous, cartilaginous, and osteoid tissue is derived from the remains of the first branchial arch. Wood<sup>3</sup> is also inclined to the view that they arise from embryonic displacements of epiblastic tissue during the process of formation of the parotid and submaxillary glands and the branchial arches. So far as it is possible to decide, those who contend for the epithelial origin have the best of the argument.

**Treatment.**—This is surgical.

Other tumors of the salivary glands are sarcoma, cases of which are described by Kelly, Lotheissen, and Schridde,<sup>4</sup> lipoma and chondroma. Von Mangoldt describes a cavernoma—a congenital telangiectatic growth, which was found associated with angioma of the overlying skin. Bidone<sup>5</sup> also reports a case and reviewed the literature fully. An echinococcus cyst has been described.

#### SYMMETRICAL ENLARGEMENT OF THE LACRIMAL AND SALIVARY GLANDS—ACHROOCYTOSIS, MIKULICZ'S DISEASE

The first complete description of this was given by von Mikulicz.<sup>6</sup> It is a chronic inflammation affecting the salivary and lacrimal glands; but there are cases, evidently of the same nature, in which the salivary glands alone are affected. Blood changes are rare; in some cases, however, the blood presents the picture of leukemia or pseudoleukemia. The lymphatic glands may be enlarged and at times there are analogous

<sup>1</sup> *Beitr. z. klin. Chir.*, 1896, xvi, pp. 181 to 256.

<sup>2</sup> *Arch. f. klin. Chir.*, 1906, lxxxi, p. 275.

<sup>3</sup> *Annals of Surgery*, 1904, xxxix, pp. 57, 207.

<sup>4</sup> *Beitr. z. path. Anat. u. z. Allg. Path.*, 1903, xxxiv, pp. 136 to 142.

<sup>5</sup> *Arch. di Ortopedia*, 1897, xiv, p. 398; 1898, xv, p. 16.

<sup>6</sup> *Münch. med. Woch.*, 1888, p. 759; *Beitr. z. Festschrift f. Billroth*, Stuttgart, 1892, p. 610.

infiltrations of the skin. The enlargement of the salivary glands is due chiefly to a diffuse lymphoid hyperplasia, and not to hypertrophy of the parenchyma proper. Von Brunn is of the opinion that the disease is due to some infectious agent carried to the glands in the blood stream. von Brunn<sup>1</sup> classifies the forms of Mikulicz's disease as follows:

I. Cases without blood changes. A. Without involvement of lymphatic glands or spleen. (a) Symmetrical enlargement of the lacrimal and salivary glands. (b) Symmetrical enlargement of the lacrimal glands alone. (c) Symmetrical enlargement of the salivary glands alone. B. With enlargement of lymphatic glands and spleen. (a) Symmetrical enlargement of the lacrimal and salivary glands. (b) Symmetrical enlargement of the lacrimal and salivary glands with infiltration of the skin.

II. Cases with blood changes. A. Grave anemia with lymphatic pseudoleukemia and aplasia of the bone marrow. B. Leukemia.

Histologically the cases are classified by Hase<sup>2</sup> into three groups:

1. Cases with hyperplasia of the normally present lymphatic tissue.
2. Cases of a chronic inflammatory character presenting tuberculous granulation tissue without caseation.

3. Cases of tuberculous granulation tissue with the presence of tubercle bacilli or positive tuberculin reaction.

A case in a negro has been reported by Ziegler.<sup>3</sup> In children the Mikulicz syndrome is not rare but is usually associated with pseudoleukemia or leukemia. According to Tileston<sup>4</sup> the term Mikulicz disease should be reserved for those cases of chronic painless bilateral enlargement of the salivary and lacrimal glands in which pseudoleukemia and leukemia can be excluded. The cases occurring in the last named disease should be classified as pseudoleukemia or leukemia with the Mikulicz syndrome. Howard's<sup>5</sup> article also contains a good bibliography.

Napp<sup>6</sup> describes a case of Mikulicz's disease in a woman aged twenty-seven years, in whom in addition to the enlargement of the lacrimal, submaxillary, and parotid glands there were submucous nodules on the lips and cheeks and in the conjunctiva. In the conjunctival nodules, which were the only ones examined, tubercle bacilli were found. On the strength of this case, Napp accepts the view of Meller that Mikulicz's disease is not a disease but a symptom complex produced by a variety of causes, such as leukemia, pseudoleukemia, a typical lymphomatosis (sarcoma), and tuberculosis. For the treatment of the condition, Pfeiffer recommends the x-ray.

**Atrophy.**—In addition to the shrinkage of the glands accompanying advancing age (senile atrophy), there is an atrophy of obscure nature that may or may not affect all of the glands simultaneously. In a case of such atrophy reported by Dubreuil-Chambardel,<sup>7</sup> the condition

<sup>1</sup> *Beitr. z. klin. Chir.*, 1905, xlv, p. 225.

<sup>2</sup> *Inaug. Diss.*, Leipzig, 1912.

<sup>3</sup> *New York Med. Jour.*, December 11, 1911. (Bibliography.)

<sup>4</sup> *Amer. Jour. Dis. of Children*, November, 1911.

<sup>5</sup> *Internat. Clinics*, 1909, 19 ser. T., 30.

<sup>6</sup> *Zeitsch. f. Augenheilk.*, 1907, 17, p. 513.

<sup>7</sup> *Province méd.*, xxi, p. 6.



revealed itself by an almost absolute smoothness of the floor of the mouth, and by hollows in the region of the parotid glands. The patient, an otherwise healthy man, aged sixty-one years, complained of dryness of the mouth. The urine was increased in amount to 2000 cc. in a day, but was free from albumin and sugar. Such an atrophy may be the underlying cause in some cases of xerostomia.

### LUDWIG'S ANGINA

This is an inflammation—a cellulitis—of the tissues of the floor of the mouth in the submaxillary region. The primary focus is usually some insignificant lesion in the mouth, as a carious tooth, tonsillitis, an ulcer, etc., the infection travelling by way of the lymphatic vessels to the submaxillary lymph glands. In 18 cases studied bacteriologically the streptococcus was found alone in 6 cases, the streptococcus associated with other organisms in 8, the staphylococcus alone in 2, the pneumococcus alone in 1, and an undetermined bacillus in 1. Males are far more often affected than females.

**Symptoms.**—The disease usually begins acutely, with slight fever, and at times difficulty in swallowing. Coincidentally an indurated swelling appears in the region of the submaxillary gland, on one or both sides which soon extends along the cellular tissue toward the chin, toward the parotid, and down toward the larynx or the sternum. The sublingual tissues form a hard congested swelling arranged like a cushion just inside the inferior maxillary bone, and force the tongue upward and toward the opposite side. The skin over the swelling, during the first four or six days, is movable, then it becomes reddened, œdematous, and adherent; at times there is crepitation. Soon an opening forms in the floor of the mouth through which a thin grayish or reddish-brown fluid is discharged; at the same time the constitutional symptoms become more severe, the fever higher, sleep is disturbed, profuse sweats, delirium, and dyspnœa appear, and the characteristic typhoidal state, due to septic infection, is developed.

Death, in the majority of cases, occurs from invasion of the larynx, the lower respiratory tract, and in some cases of the lungs. The mortality is high; of 106 cases collected by Thomas, 43 died.

**Treatment.**—This is surgical; the best incision being that of Delorme, over the submaxillary gland and parallel with the lower jaw.



## CHAPTER III

### DISEASES OF THE ŒSOPHAGUS

BY JOHN McCRAE, M.D. (TOR.), M.R.C.P. (LOND.)

**Descriptive.**—The Œsophagus begins at the upper border of the cricoid cartilage and ends at the cardiac orifice; it measures, on an average, 24.4 cm. (about nine and three-quarter inches); at birth it measures 8 cm.; at the level of the sixth cervical cartilage it lies in front of the vertebræ, then it comes slightly forward, and at the seventh dorsal vertebra it bends slightly to the right, then to the left to reach the opening through which it passes the diaphragm. It enters the stomach at a point corresponding to the origin of the twelfth left rib from the twelfth dorsal vertebra, and the cardia lies about 40 cm. from the upper incisor teeth. The Œsophagus is divided, for descriptive and other such purposes, into a cervical part 5 cm. long, a thoracic 18 cm. long, and an abdominal 2 cm. long. If it is desired to know the distance from the incisor teeth to the cardia, Rosenheim gives the following rule: Take a point 2 cm. below the most prominent part of the occipital protuberance, measure from it to the origin of the twelfth rib, and add 7 cm. (from uvula to upper teeth) for the total figure. It is probable that for the most part the walls of the tube lie in contact with one another, but it is yet undetermined whether or not the cardia lies open when the organ is at rest; Killian considers that the cricopharyngeal muscle forms a sphincter or mouth of the Œsophagus, just as the cardia is that of the stomach.

The Œsophagus is lined by stratified pavement epithelium. In the upper part the muscularis is composed mostly of striated, and in the lower half of unstriated muscle fibres, although the demarcation is not distinct. Mucous glands in rather scanty numbers lie in the submucosa and open by ducts which pierce the muscularis mucosæ; glands of a different kind are found between the level of the cricoid cartilage and the fifth ring of the trachea, lying superficial to the muscularis; these glands contain not only mucous cells, but also cells similar to the parietal cells of the glands of the stomach; and at times typical stomach epithelium is found aggregated in areas of considerable size, which on superficial examination resemble shallow ulcerations, of which the true nature becomes apparent only on microscopic inspection. These are found in 3 to 6 per cent. of all cases. In the lower part of the Œsophagus are the cardiac glands, which are similar to the cardiac glands of the stomach.

The arterial supply consists of an anastomotic network, which is supplied from above downward by the inferior thyroid, the posterior bronchial arteries, and the Œsophageal branches of the aorta. The lower end is supplied by the left coronary artery of the stomach, and

anastomoses occur from the inferior phrenic vessels. The venous out-flow travels by three main channels, of which the first leads to the inferior vena cava by the diaphragmatic veins; the second leads to the superior vena cava by way of numerous branches, the inferior thyroid, the pericardial, the posterior mediastinal, the intercostal, and the diaphragmatic veins. These last lead to the azygos or to the vena cava itself. The third channel, most important in its relation to varices of the œsophageal veins, leads by way of the left coronary vein of the stomach to the portal system. The venules leading to all three channels are closely interlaced throughout the œsophageal walls.

The lymphatics of the œsophagus lead from the upper part to the deep cervical nodes lying in the vicinity of the bifurcation of the carotid artery, and from the inferior part to the nodes of the posterior mediastinum, as far as the diaphragm.

The nerves supplying the œsophagus are, above, the recurrent branches of the vagi, and below, a plexus formed of branches direct from the trunks of the vagi, into which enter branches of the sympathetic.

The question whether or not absorption occurs from the œsophagus is not yet authoritatively settled; probably the œsophagus can absorb, but rarely obtains opportunity therefor.

**Methods of Examination.—Palpation.**—This may give information of a tumor high up in the œsophagus, and the glands connected therewith may sometimes be felt, or a diverticulum full of food material may be palpated, and sometimes emptied by pressure; but the application of these methods is necessarily very limited.

**Percussion.**—Percussion will prove useful very rarely; it may assist in the determination of a large diverticulum or tumor.

**Auscultation.**—This gives little satisfactory information; over the whole extent of the œsophagus, when fluid is swallowed, a gurgling sound may be heard, which may cease at the level where an obstruction exists; the sounds may be heard over the neck, down the left side of the spine, and finally at the angle made by the left costal margin with the xiphoid cartilage. Very commonly at this point, six or seven seconds after swallowing, a sound is heard which is interpreted by some as fluid passing through an almost closed or half-closed cardiac orifice, by others as a sound produced in the stomach. In some people, immediately after swallowing, a sound is heard which is taken to indicate the passage of fluid through the open cardia. Succussion sounds are sometimes heard in large diverticula.

**Stomach Tube, Sounds, Bougies, etc.**—These are very useful as instruments of examination, as well as in the treatment of œsophageal disease. The best for a preliminary examination is the soft-rubber tube, and if, subsequently, sounds are necessary, the graduated, gum-elastic English sounds, which when heated become flexible and can be bent to the desired shape, may be used. Briefly stated, the rules for all such examinations are these: Ostentatious cleanliness beforehand is necessary, so that nausea or disgust through mental channels is not excited; let the patient sit with the head thrown slightly forward and the chin raised; if necessary, paint the pharynx with 10 per cent. cocaine solution. Do not put the

fingers in the patient's mouth unless it is necessary; glycerin as a lubricant may generally be dispensed with, the tube being best taken last from cold, clean water; if sounds are used, from warm water; direct the patient to take full, deep breaths, and enforce this upon him at any time he becomes excited. Contra-indications to the use of the tube are as follows: *Absolute*: Aneurism, recent hemorrhage, recent corrosion, or ulceration. *Relative*: Advanced arteriosclerosis or cardiac disease, acute œsophagitis, or cirrhosis of the liver when varices may be suspected.

**Œsophagoscope.**—The findings from this, to the practised eye, are of the utmost value; the discomfort it causes the patient and the difficulty of its use by the physician have not yet allowed its widespread employment. Even with the development of fluoroscopy, there yet remains a great field of usefulness for this instrument.

**The Fluoroscope.**—In the examination of the œsophagus, the use of the fluoroscope is constantly becoming more widespread, and while the great majority of cases examined indicate a freely moving and properly timed passage of the swallowed material, the method is extremely useful in the detection of stenoses of different kinds, and, occasionally, of diverticula. It is usual to employ a barium sulphate or bismuth mixture which is swallowed by the patient at the instant ordered. In health the narrow mass of the fluid is seen quickly to descend and pass into the stomach, whereas if there be hindrance to such passage it is seen to stop and change its form at the level concerned. Semisolid food mixed with barium sulphate or bismuth may be observed even better, and under ordinary circumstances it does not happen that sufficient material adheres to the walls of the gullet to cast a shadow. Gelatin capsules of the ordinary type (8 to 10 mm. in diameter) filled with barium sulphate or bismuth, are also used, and it is to be remembered that these almost invariably momentarily stick opposite the top of the arch of the aorta, and, indeed, may not pass this point until the patient has made repeated swallowing efforts; this must not be taken to indicate a stricture. In the case of organic stricture, the barium sulphate or bismuth remains in the œsophagus sufficiently long for a radiogram to be made. It has been observed when stenosis is organic that liquid food may be seen to leak away slowly through it; whereas if the stenosis be a spasmodic one, when it relaxes, the entire mass of food is seen to drop away at once. In malignant growth there is sometimes a zig-zag lumen outlined by the barium or bismuth adhering to it. The œsophagus is best examined with the fluoroscope when the patient is in the oblique position, that is, with the view-point from the patient's right front toward his left back.

### CONGENITAL MALFORMATIONS

These are not common, and are clinically of so little importance as to deserve the merest mention; they consist, for the most part, of a series of variations dependent on the fact that embryologically the œsophagus and pharynx have a common origin, separation being com-



plete at the fifth week. With failure of this separation, œsophago-tracheal fistulæ of varying size arise; the two tubes may actually form but one in part of their course. Fistulæ<sup>1</sup> or more properly, sinuses, may be found on the anterior wall, each having its own muscle coats. Œsophageal cysts<sup>2</sup> may arise from separation of such sinuses, or, again, may be true retention cysts from mucous glands.

The continuity of the œsophagus may be interrupted by a stenosis or obliteration. Thus the tube may be open above and below, and its central part may be represented by a mere cord. Either the upper or the lower segment may open into the air passages. It sometimes happens that the œsophagus, although patent, opens into the trachea, and aspiration pneumonia is thus produced before any suspicion can arise of abnormality. Two gullets have been known to exist side by side. The anomalies that are congenital and consistent with life are referred to in different parts of this article.

### INFLAMMATION OF THE ŒSOPHAGUS

**Acute Œsophagitis.**—**Etiology.**—This is infrequently found at autopsy, but is probably much more frequent in life. It occurs by extension of disease from the pharynx or stomach, or from other nearby organs, is excited by mechanical irritation, such as a foreign body or a rough sound, by hot liquids, corrosives, or other chemical irritants, and occurs as an accompaniment of inflammation of mediastinal tissue or other parts near but external to the œsophagus, and in various acute diseases, as diphtheria, scarlatina, variola, measles, pyemia, and typhoid fever.

It is remarkable that the œsophagus has so great an immunity to the spread of infections from the pharynx; it must have impressed anyone who has had the opportunity of seeing autopsies upon patients who have died of scarlet fever or diphtheria, that when the œsophagus is laid open its pale, healthy surface contrasts vividly with the reddened hyperemic pharyngeal structures, and that the infection stops short at a well-defined line which marks the level at which the walls of the gullet appose. Cases in which the inflammation spreads to the œsophagus and even ulceration of the same<sup>3</sup> are observed at times, but are the exception. The food and saliva must constantly wash down infective material from the mouth, but this remains only momentarily; there must be another explanation, which is perhaps that the œsophagus is a strongly resistant part. Even when corrosives are swallowed it often escapes with less injury than the pharynx or the stomach, and it is certain that the constant passing of rough particles of food seems rarely to tear the œsophageal membrane.

**Special Pathology.**—Many different forms and degrees of inflammation are recognized, as catarrhal, follicular, ulcerative, phlegmonous, exfoliative, or necrotic, the relation of which to one another is close. In the

<sup>1</sup> Ciechanowski and Glinski, *Virchow's Archiv*, Band xcix, 420.

<sup>2</sup> Kern, *Virchow's Archiv*, Band cci, 135.

<sup>3</sup> Rolleston, reported in *Schmidt's Jahrbuch*, 1912, Band ccxv, Heft 1.



ordinary catarrhal form the wall is reddened, and there is excess of secretion with desquamation as a sequence. This is the usual result of fluid too hot or mildly irritative, not to say corrosive, or as adjunct in the vicinity of foreign body or new-growth, although here it is of little clinical significance. Such an œsophagitis may be the result of a passive hyperemia from cardiac disease, although the long continuance of such a cause generally operates to place it in the class of chronic disturbance. This simple form may be associated with the exanthemata, or the membranous type may be observed where an actual fibrinous membrane, not to be confounded with the desquamating dead layers, is present. Very rarely, the membrane is truly diphtheritic, which obviously may lead to ulceration. The pocks of variola have been frequently found in the œsophagus, Wagner finding them in about 13 per cent. of a large series. Various other forms of disease are occasionally noted; in the condition termed follicular œsophagitis the mucous glands of the upper part of the tube can be distinguished as lumps, sometimes of the size of 6 or 7 mm. in diameter, which exude abundant mucus through the dilated duct on pressure; microscopically, such glands are found to have undergone a mucoid degeneration, to be surrounded by a zone of inflammatory infiltration, and each area may finally form an ulcer.

Allied to this condition is the formation of retention cysts, when the thickened epithelium occludes the duct; these cysts, which may attain a diameter of 1.5 cm., have been known to become infected, and the result is the formation of an abscess, circumscribed but tending to extend its boundaries. Should this occur, we have an example of purulent or phlegmonous œsophagitis, although the etiology of the latter is generally other than this. It most frequently happens in the upper part of the tube subsequent to the lodgement of a foreign body, the action of a corrosive, or by extension of an extraneous inflammation. Several cases are recorded in which, some days after drinking lye, mucosa and submucosa have been shed as a membrane. Dorr, indeed, found one such piece 30 cm. long, this doubtless including parts of the pharyngeal mucosa and Neisser<sup>1</sup> has lately reported another case in which the cast was 30 cm. in length. When abscesses form they are apt to undermine the mucosa and lead to the establishment of sinuses, or even of fistulæ into the respiratory tract. The possibility of the causation of peri-œsophageal abscesses in this way is also to be remembered. The course of the infection may, however, be in the other direction, and peri-œsophageal abscess may undermine from the outside, or the disease in the œsophagus may be the result of extension from a perichondritis, a vertebral abscess, suppurative lymph nodes, or even from empyema. In such cases the mucosa may be finally perforated. Such an accident is not necessarily fatal; here belong those wonderful cases in which large pieces of the lining, sometimes the entire lining of the tube, have been cast off in one mass, although the cases were not instances of corrosive poisoning. Where a long-continued inflammation has existed, strong retching or vomiting has separated the layers, and cure is reported after

<sup>1</sup> *Berl. klin. Woch.*, Jan. 3, 1910.

a cast 13 cm. long had been so expelled (Stern). Birch-Hirschfeld reported long ago a case in which a 20 cm. cast was expelled three days after the onset of the first œsophageal symptoms; the patient promptly recovered. In the necrotic form ulceration occurs alternating with fibrin-covered areas; on these latter an actual membrane often forms, and the ulcerations may give rise to hemorrhages; this combination has been reported as following many of the acute infectious diseases and in cases of sepsis. In the Royal Victoria Hospital autopsy series a girl, aged nineteen years, dead of septicemia, showed in the œsophagus multiple irregular ulcerations, the result of thromboses of small vessels. One of these perforated into the left pleura, and caused a hemorrhagic pleurisy.

*Corrosive Œsophagitis.*—Œsophagitis from corrosives may be referred to, although it is obvious that the pathological condition will fall under one or other heading already dealt with; a single case of corrosion may combine several different forms at the same time in different parts of the tube. Where the corrosion is comparatively mild, the epithelium is whitened and converted into a rough membrane peeling off in patches, but leaving an apparently intact membrane below it. The epithelium may be colored according to the corrosive used. Thus, sulphuric acid generally blackens, carbolic whitens, and nitric acid gives a yellow color to the surface. When the corrosive is a very severe one, the mucosa is converted into a dirty gray slough, peeling off irregularly from a reddened, hemorrhagic surface, which is greatly inflamed; the muscular coat is in these cases extremely flabby and the tube sags. A little later these tissues become black and gangrenous-looking. Should death not occur soon, suppuration and ulceration in any direction may happen, and at the best, healing will be attended with the highest degree of stricture.

*Infective Œsophagitis.*—In the specific infections, besides diphtheria and variola mentioned above, the ulcers of typhoid fever are occasionally found in the œsophagus, the latter happening once in 83 autopsies upon cases of typhoid fever in our series. Thrush is found as a result of extension from the mouth, but in most instances is of little importance.

**Symptoms.**—When corrosives have been swallowed, the history and inspection of the pharynx generally make the case clear. There is usually severe pain along the course of the gullet, dysphagia, and expectoration of mucus, often bloody. Thirst is extreme. In the severest cases there may be no pain. With regard to other forms of œsophagitis, with lesions of so variable intensity, it is not easy to set down a train of symptoms that will be accurate for all; it is of the utmost importance to know if damage has been done to the gullet by food material or other foreign body. Apart from the history, the most dependable symptom is inability to swallow or pain in swallowing; pain may exist when the head is moved violently, especially backward, and when the œsophagus can be reached from the neck, pressure may elicit tenderness. There is often thirst, and sometimes regurgitation of swallowed material which may be coated with mucus. Hard, dry food, or very hot or very cold fluids, will give more pain than less irritating material. If a sound

be used (it is usually contra-indicated), great pain is caused, which is apt to remain for a considerable time after its withdrawal.

**Sequelæ.**—Slight degrees of inflammation are almost certain to disappear completely, and severe degrees, with ulceration, are equally certain to be followed by stenosis. Any inflammation may progress and lead to the ulcerative or phlegmonous form, which in turn may give rise, with or without perforation, to peri-œsophageal abscess. If the inflammation leads to perforation, especially low down in the œsophagus, the respiratory tract, trachea, bronchus, or pleura, is likely to be invaded by the escaping material.

**Diagnosis.**—œsophagitis, especially if it occurs in the course of some severe disease, will generally be overlooked. Excessive pain from the use of tube, sound, or œsophagoscope, should suggest the possible existence of œsophagitis and the immediate discontinuance of its use.

**Treatment.**—In the severe forms, such as occur in the swallowing of corrosives, oil may be given, but after this the gullet is to be left absolutely alone, and fluids should be given by the rectum; should this not be possible, gastrostomy may be required. If the secretion is very great, and pain and nervousness cause the patient to make constant swallowing efforts, morphine had better be employed; ice-bags may be applied to the stomach, neck, or back; hot applications also are serviceable.

Thrush requires mild antiseptic drinks. For the slighter forms of œsophagitis little treatment is necessary if it be remembered that the blandest and most mucilaginous forms of food are the best, and that all the œsophagus needs is a little time, and complete freedom from irritation; demulcent drinks are of great use; ice may be sucked and cold drinks in small quantities are grateful, and presumably do no harm; occasional draughts of bismuth emulsions are useful. The use of tube, sounds, or bougies is contra-indicated in the acute stage. The greatest degree possible of physiological rest is the solution of the problem.

**Chronic œsophagitis.**—It is largely an arbitrary matter as to what we designate acute or chronic œsophagitis. Reference will be made here to certain chronic inflammations, and to several diseased conditions, such as rupture, dilatation, and diverticulum, which have some relationship to the degenerations of the œsophageal wall, whether these are actually caused by inflammation or not. Chronic œsophagitis is found chiefly in drunkards, occasionally in heavy smokers, and as a result of extension of pharyngitis or gastritis. Occasionally it may follow a repeated or long-continued congestion brought about by disease of the heart or lungs. The condition is often found at autopsy, and is generally overshadowed during life by the symptoms of more apparent lesions.

**Special Pathology.**—The most frequent form of chronic inflammation is that which shows a series of grayish streaks corresponding to the crests of the longitudinal folds into which the tube falls when at rest. Where the sides of the rugæ lie in apposition this membrane is not apparent, and the mucosa is generally dusky red or bluish, the attrition serving to rub off the membrane as soon as formed. The membrane appears to consist of degenerated superficial layers with little or no fibrin. This picture differs little from that of acute catarrhal œsophagitis,



except that the lividity of the wall is more extreme. This low grade of disease may exist for a long time without giving rise to any symptoms, but long persistence leads to mucosal thickening and sometimes to a granular appearance of the membrane. Next to this, and closely allied to it, is the so-called leukoplakia, in which there are white, yellow, or gray plaques of irregular size and distribution, overlying and alternating with thickened and reddened mucosa and submucosa; these areas are slightly harder and more raised than the rest of the mucosa, and are underlaid by inflammatory infiltration. This is precisely the same condition that is well known in the mouth, and it is thought to have some etiological force in the causation of carcinoma, although the figures cannot be said to be conclusive. The strongest causative factor in the production of leukoplakia of the œsophagus is alcoholism. There is found also the form of œsophagitis in which the mucosa is dark red and granular, without any evidence of fibrin or membrane. All these varieties are of the same significance, and seem to occur under similar conditions.

Chronic œsophagitis may be characterized by a gray, œdematous mucosa as well as by a hyperemic one; there may be an increased quantity of mucus secreted; the thickening of the mucous layers occurs at times so irregularly as to give rise to papillate or polypoid outgrowths. As an accompaniment of this, the openings of the mucous glands are at times evident. Ulceration does not appear to be frequent, save in the most severe cases; pigmentation of the mucosa is uncommon, and atrophy of the mucosa probably does not occur, save in old age.

**Symptoms.**—The most common complaint is uneasiness, scarcely amounting to pain, in swallowing; it is rarely severe, although this depends entirely on the degree of the lesion, and is generally referred by the patient to the upper part of the œsophagus, and by the observer to the pharynx, which is usually inflamed.

**Sequelæ.**—Because the infective agent is less virulent or the tissues more habituated, chronic inflammation is less likely to lead to severe destruction and subsequent stenosis than in the case of acute inflammation. It is likely that chronic œsophagitis precedes unexplained cases of rupture and dilatation; it is, therefore, far more important in the light of those lesions to which it predisposes than for its own sake.

**Treatment.**—Various forms of treatment have been advocated, but the condition will continue to be, in most cases, untreated. The removal of an exciting cause, such as alcohol or tobacco, is necessary; extremely hot or pungent foods are to be avoided; it is possible by demulcent fluids to smear the œsophagus with material which will adhere to its walls for a time; the passage of a tube to apply such fluids or pastes is admissible. A useful method of applying astringent drugs to the œsophageal wall is the daily use of a soft tube smeared with a paste which is solid at ordinary temperature but melts at body heat. Such a paste can be made of cacao butter mixed with tannic acid (10 per cent.) or silver nitrate (5 per cent.). The tube is allowed to remain ten or more minutes until the paste is melted and transferred to the wall of the œsophagus. Solutions of cocaine (1 to 2 per cent.) and eucaine (3 to 4 per cent.) are used to allay pain, and solutions of tannin and silver nitrate



(1 per cent.) are advised. If such solutions are used, swallowing in the recumbent posture seems advisable.

**Ulcers of the Œsophagus.**—It is not exactly rational to separate these from the foregoing inflammations. Ulceration may occur as a step in the process of œsophagitis, but several forms of this lesion yet remain to be described. These are the so-called decubitus ulcers, pressure ulcers, peptic ulcers, and uremic ulcers. At the same time that these are separated from acute and chronic œsophagitis, it is done with no intention of suggesting that we are dealing with other than inflammatory processes, or at least those modifications of inflammatory processes which we are accustomed to call degenerations.

**Decubitus Ulcers.**—These are found in emaciated persons who have suffered from exhausting disease. They are usually shallow, round erosions, with little or no surrounding reaction, and are situated on the anterior and posterior walls of the œsophagus, at the level of the cricoid. Each is the counterpart of the other, and they are caused presumably by the attrition of the apposed walls while the patient lies recumbent, the œsophagus being pressed between the cartilages of the larynx and the vertebral column. They give rise to no symptoms.

**Pressure Ulcers.**—These may appear on the inner surface of the œsophagus as a result of compression from without by an aneurism or other mass. The lessened blood supply from the pressure doubtless lowers the resistance of the part, so that these are closely related to the foregoing.

**Peptic Ulcers.**<sup>1</sup>—So long as the etiology of gastric ulcer remains obscure, it is rational to consider peptic ulcer of the œsophagus as a sequence, although perhaps a distant one, of inflammatory conditions of the wall. It occurs generally in the lower part of the gullet under conditions similar to those in which gastric and duodenal ulcers occur, which, in fact, it often accompanies. Yet it must be said that it has generally been reported in elderly, alcoholic men, which fact alone casts doubt upon the exact parallelism. It may be said that the prevailing opinion is in favor of peptic ulcers being the result of a combination of thrombosis of the area affected, with subsequent digestion.

**Symptoms.**—The condition causes difficulty in swallowing, sometimes vomiting of blood, occasionally a fatal hemorrhage, and the course, apart from the last-named accident, is likely to be a chronic one. Diagnosis is difficult and the malady must be distinguished from varices of the œsophagus and ulcer of the stomach.

**Treatment.**—This is exactly that of acute œsophagitis, gastrostomy being the most satisfactory method.

**Uremic Ulcers.**—Ulcers of the œsophagus occur in uremia, and are doubtless comparable to the better-known but equally ill-understood ulcerations found in the colon in uremia; in thirteen cases of uremia in the Royal Victoria Hospital, œsophageal ulcerations were found twice.

<sup>1</sup> For literature, see Kappis, *Milth. a. d. Grenzgeb. d. Med. u. Chir.*, 1910, xxi, p. 746.

## RUPTURE OF THE ŒSOPHAGUS

Rupture of the œsophagus is rare, but has happened in a well-authenticated series of cases. Cohn<sup>1</sup> has collected all the cases available.

**Etiology.**—Much discussion has occurred as to whether a healthy œsophagus ever ruptures; the writer's belief is that it does not. At the same time, in some cases that have been carefully examined, no trace of disease has been found; with regard to this, it must be borne in mind that many degenerations are not evident to the examining eye, even in heart muscle, where we are accustomed to look for them.

"Spontaneous" rupture of the œsophagus has always occurred with a high internal pressure, such as is caused by the passage of a very large bulk of solid or fluid, coincident with a strong diaphragmatic contraction; thus, it is oftenest during severe retching or vomiting that the viscus gives way. Zenker considers that a rapid degeneration of the wall of the œsophagus is produced by the presence of a pepsin-containing fluid regurgitated from the stomach, which remains at body heat, at the same time that a condition of weakened œsophageal circulation is present; this degeneration is the predisposing, as the high intra-œsophageal pressure is the effective, cause of "spontaneous" rupture. Such degeneration could be effected only upon the internal layers, and it is extremely likely that an equally effective or more effective cause would be a degeneration, inflammatory, or other, of the muscular wall. Adhesions which tie the œsophagus to surrounding structures are important, as they lessen the elasticity of the tube.

**Symptoms.**—Rupture of the œsophagus is characterized by severe, sudden pain in the chest, a choking sensation, retching or bloody vomit, and collapse. All of the cases have proved rapidly fatal, although in some death has been sufficiently delayed to allow the signs of interstitial emphysema of the mediastinal tissue to develop.

## IDIOPATHIC DILATATION OF THE ŒSOPHAGUS

Idiopathic dilatation of the œsophagus will be dealt with when the subject of ectasia is taken up; suffice it to mention here that there are certain diffuse dilatations for which a cause cannot be assigned; in the absence of cardiospasm and other stenoses these are thought to be due to atonic degeneration of the wall.

## INFECTIVE GRANULOMATA OF THE ŒSOPHAGUS

**Tuberculosis.**—Tuberculous disease of the œsophagus is rare, but may occur by inoculation with tuberculous material which is swallowed; more commonly than this, the disease appears as areas of ulceration,

<sup>1</sup> *Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1907, xviii, p. 295.

which have extended from the bronchial lymph nodes, the trachea, occasionally the dorsal vertebræ, or even the lungs; or, finally, the œsophagus may share in a general miliary tuberculosis. Thus it will be seen that the œsophagus suffers late in the disease, when any symptoms to which it might give rise are overshadowed by others, so that the diagnosis can be made but rarely. There is no certain symptom or group of symptoms, although with advanced disease elsewhere severe pain on swallowing suggests its presence. Guisez and Abrand<sup>1</sup> have collected a sufficient number of cases to permit of a classification into three types; first, those arising by continuity from outside the œsophagus, second, ulcerative, by hematogenous or lymphogenous infection, and third, those attended by sclerosis and stenosis.

**Syphilis.**<sup>2</sup>—Syphilitic disease of the œsophagus is rare, and takes the form of stenosis, gumma and ulceration. Therapeutic evidence in favor of its existence, namely, that the disability disappears after the use of antisyphilitic measures, is apt to be inaccurate. In the treatment of ulcer or stenosis, constitutional treatment is even more important than local measures.

**Actinomycosis.**—Actinomycosis and blastomycosis of the œsophagus have been described, and trichiniasis also occurs.

### NEUROSES OF THE ŒSOPHAGUS

There is a tendency to think that neuroses exist without organic lesions but in the œsophagus, as elsewhere, it is well to remember that some lesion may exist which is a point of origin for the stimuli that call forth the symptoms. The lesion may be, often is, quite inconsiderable and out of proportion to the symptoms it excites, but the results of treatment will at times be much better if it be borne in mind that such may exist. In many cases not the slightest deviation from the normal state is to be detected.

**Sensory Neuroses.**—Disturbance of the sensory functions of the œsophagus usually takes the form of hyperesthesia and paresthesia; anesthesia is said to occur after such infections as diphtheria, but is very difficult to determine. The two former conditions are more definite, and hyperesthesia is frequently present, although it is often not a neurosis but an accompaniment of actual disease, such as inflammation or new-growth. Paresthesia takes very different forms, such as pain in swallowing, a feeling as if the tube were closed, a sensation of weight, a feeling as if there were a foreign body in the œsophagus, and finally the sensation of a lump which is usually called the *globus hystericus*, which last is described at times as ascending, and at others as descending. The surface of the œsophagus sometimes is described as feeling "rough;" in any of these conditions the distress may be less during the taking of food, although this is by no means to be depended upon, for the neuroses may

<sup>1</sup> *Rev. de Chir.*, July, 1909, p. 23; see also Gardère, *Gaz. des Hôp.*, 1910, lxxxiii, 15; and Staehelin-Burckhardt, *Arch. f. Verd.-Krankh.*, 1910, xvi, p. 484, who cites references.

<sup>2</sup> *Progrès Méd.*, 1910, No. 10, p. 131.



be severe enough to lead to marked inanition by starvation. These paresthetic states are often the accompaniments and sometimes the results of hyperacidity and allied conditions of the stomach that are called neuroses, and a familiar form is that described as "burning," which may extend as high as the pharynx; it must be kept in mind that this symptom is often the result of insufficiency of the cardiac orifice and the consequent regurgitation of (hyper) acid fluid. The use of the tube, sound, or œsophagoscope may demonstrate that there is no gross organic disease, and the recognition of a neurosis of the stomach, or an unbalanced state of the nervous system in general, may be a useful guide to the recognition of the true state of affairs.

**Diagnosis.**—It is not easy to make useful suggestions as to the diagnosis of the neuroses, as the symptoms and the organic diseases that may be simulated are so numerous. In general, it may be said that the greatest care is necessary that organic disease be not overlooked, and the more unusual neuroses can be determined only after careful exclusion.

**Treatment.**—This requires that the general cause be recognized and the state of the nervous system in general be improved; because of the reality of the distress to the patient, symptomatic treatment is frequently necessary, and may take the form of regularly administered drinks, such as weak tea, soda-water, weak solutions of tragacanth or acacia; in bad cases these may be followed by opium in small doses, tr. opii, ℥x (cc. 0.6), with aqua laurocerasi, ℥xx (cc. 1.2) or 0.25 to 0.5 per cent. solution of silver nitrate, of which half a dram in water three times a day will usually suffice. Weak solutions of cocaine (1 to 2 per cent.) may be used by the help of the stomach-tube and removed after ten minutes' application.

**Motor Neuroses.**—The motor neuroses are more important than the sensory, and are practically confined to spasm in various situations. A few cases of merycism, or rumination, do occur, which are evidently connected with a relaxation of the cardiac orifice; some cases have been quoted to show that a real "fore-stomach" may occur as in ruminants, this hypothesis depending on the presence of a sac at the lower part of the œsophagus just above the cardia. In a case recently reported,<sup>1</sup> the sac when distended, attained a width of 23 cm.

Before going on to speak of spasm proper of the œsophagus, it may be mentioned that some consider the *globus hystericus* to be spasm in its lowest degree; that is, that an actual point of contraction may pass up and down in a kind of peristaltic action of the tube. Whether this be the case or not, mild temporary spasms, which last but for a moment do exist, and almost as soon as the patient recognizes that the food does not pass freely they yield, just as their better developed brethren yield to the application of the tube or sound. The patient has a momentary sensation that the food is obstructed, and that is all. It is only when the spasm is severe and consistent that there is damage wrought.

**Etiology.**—Spasm which is purely neurotic, called idiopathic, exists chiefly in young adults, rarely in children, and oftenest in females.

<sup>1</sup> May, *Munch. med. Woch.*, October 12, 1910.



Excitable, nervous people and hysterical persons are the ones most frequently afflicted, and a shock, fright, or anger is often the signal for an attack; the older writers seldom fail to mention the dread of hydrophobia as an excitant. Pregnancy appears at times to have this disturbing effect. There are also cases which are not idiopathic but reflex, occurring generally in the same kind of people as the idiopathic. As a result of errant stimuli, excited by a diseased condition of structures which have a related nerve supply, or stimuli arising in a functionally disordered central nervous system, or even stimuli originated by some slight lesion of the œsophagus itself, the motor nerves of the œsophagus carry impulses which result in a spasmodic contraction of the muscles, occurring most often at the upper part of the tube or at the cardiac orifice of the stomach. Notwithstanding the reality of the muscular contraction, the cases which have died with a spasmodic stenosis have failed to show any sign at autopsy, although one or two reported cases have indicated a possible persistence of the condition after death. The most usual site of a spasmodic closure of the œsophagus is at the cardia, and whether this be considered œsophageal or gastric matters not for practical purposes. These stenoses are found in various parts of the tube, and the spasm is not necessarily always at the same place. When an organic stenosis exists, a spasmodic stenosis at the same or a different part of the tube may be superadded.

An extreme degree of spasm of the œsophagus is described under the name of (Esophagismus). A striking case, recently reported,<sup>1</sup> details that extremely prostrating attacks with retching, profuse salivation, and intense pain under the lower part of the sternum, were relieved by the administration of atropin.

While œsophageal spasm is under consideration, it is well to remember that it tends to be followed by dilatation of the tube above the site of spasm, and that although the spasm may be relieved, there is a great tendency to permanence of the sacculation. Myer<sup>2</sup> considers that such dilation occurs in patients who have a congenital asthenia, such as is often exhibited by the occurrence of enteroptosis.

**Symptoms.**—The slighter degrees of the disease show a sudden, variable inability to swallow; one cannot predict what kind of food is likely to excite it; in some it is hot, in some cold, in some solid, and in some liquid; at times the larger the mass the more easily it is swallowed. The attempts at swallowing are often audible, and the attention of others is apt to increase the difficulty experienced by the patient. Variability of symptoms is very noticeable. Emaciation is absent in the slight or moderate cases. In severe cases dysphagia may be complete, so that regurgitation of material eaten some time before may happen, the material indicating by the absence of hydrochloric acid or pepsin that it has not reached the stomach. The act of attempting to swallow is accompanied by dragging pain in the retrosternal region, and fluids are sometimes more difficult to swallow than solids. Dyspnœa, oppression, palpitation of the heart,

<sup>1</sup> Tibbetts, *Practitioner*, London, August, 1911.

<sup>2</sup> *Jour. Amer. Med. Assoc.*, October 29, 1910, lv; see, also, Myer and Carman, *ibid.*, 1912, lix, p. 1278.

syncope, and even convulsions may accompany the attack. The condition may be momentary or continue for hours, and the liability to recurrence has been known to last through half a long lifetime.

**Diagnosis.**—This is important, and must be made from inflammatory narrowing, stenosis by malignant growth, general or partial dilatations, impacted foreign bodies, or even from the pressure of a mass outside the œsophagus. A goitre has been known to exert such pressure. To distinguish spasm from diverticulum, it must be remembered that in the former there can be no real ructus or vomiting of stomach contents during the spasm, but the tube alone can be emptied; with a diverticulum the stomach may regurgitate food, although the diverticulum be full. The fluoroscope is essential for such observations. The age, sex, and character of the patient are of importance, and the most useful single characteristic of spasm of the œsophagus is the variability of the symptoms. Very complete information may be obtained from the use of the stomach tube, which is sometimes found to be grasped by the stricture, most often at the cardia; after a few moments or minutes the spasm passes off, and the tube passes easily; if a sound be used it ought to be of fairly large calibre, such as 1 cm. diameter, but information is at times subsequently obtained by the different diameters of the sounds that will pass on different occasions in the same patient. The sound is generally the quicker, and from the physician's stand-point more satisfactory than the tube. Atropin, gr.  $\frac{1}{100}$  (gm. 0.0006) administered a few minutes before passing the sound will sometimes tend to relaxation of a spasmodic stricture. It must not be forgotten that organic lesion may coexist with spasmodic stenosis. If large sounds do not pass, it is rational to give an anesthetic, and if it pass during anesthesia, the condition is spasmodic. Stenosis which disappears after the use of antispasmodics, the sound, or galvanism can be almost certainly determined as spasmodic. The sound must be used with great care, for false passages are occasionally made, and Kümmel<sup>1</sup> reports two fatal cases, in which by reason of the absence of external hemorrhage and lack of subjective disturbance, the accident was not observed at the time.

**Treatment.**—In this it is obvious that, as in other neuroses, the main object is to render the general health and tone of the nervous system so good that the spasm will cease to occur; if a local cause exist, to which the spasm may be attributed, it should be removed; such causes have been found in chronic disease of the tonsils, the presence of a foreign body in the ear, intestinal parasites, and many diverse slight derangements to which attention would scarcely be directed in time of health. The food which the patient thinks the best is desirable, although the character of this is subject to change. Generally, warm or sweet fluids are less apt to excite spasm than cold or acid ones.

In cases that are at all severe the use of the tube or sound is necessary, and it is often notable that although the use of the sound will usually overcome the spasm, it will not necessarily prevent its recurrence; when the spasm has yielded to the sound or the tube, it does not always follow

<sup>1</sup> *Deutsch. med. Woch.*, 1911, xxxvii, No. 46.

that food taken immediately will be allowed to pass, but such is generally the case. The tube, or preferably the sound, should be inserted gently until it meets the obstruction, where it is sometimes grasped; if grasped, it should be allowed to remain until released, which generally happens in a few moments or minutes; if not grasped, a gentle equal pressure should be kept up until the obstruction is felt to yield. If the spasm be frequent, it is of the very greatest importance that the patient's nutrition be kept up; in severe cases, the performance of a gastrostomy for temporary use is at times justified.

Many ingenious appliances have been devised for the dilatation of spasmodic stenoses, most of which are based upon the use of a rubber bag, placed in the area to be stretched and subsequently distended by fluid with observation of the pressure obtained.

## OTHER ŒSOPHAGEAL AFFECTIONS ARISING FROM THE NERVES

**Paralysis.**—This is known as a sequence of diphtheria, and is characterized by partial or complete inability to swallow, the first indication of its existence frequently being the regurgitation of liquids through the nose, due to an associated paralysis of the palate. In an uncomplicated paralysis of the œsophagus the food bolus sticks, and the gullet is as little able to regurgitate it as to pass it downward. As soon as it is recognized, the greatest care must be exercised lest food be aspirated into the air passages. If the physician is in doubt as to the efficiency of the muscles of deglutition, tube-feeding must be instituted. The condition is curable only by time, although the constant hypodermic injection of strychnine, gr.  $\frac{1}{20}$  (gm. 0.003) thrice daily, appears to be of advantage.

**Herpes.**—At least one well-authenticated case of herpetic eruption<sup>1</sup> in the œsophagus has been reported, but it is worthy of mention rather as a curiosity than as a condition likely to be met, as is also pemphigus,<sup>2</sup> which may be mentioned as an actual happening.

## DILATATION OF THE ŒSOPHAGUS

Diffuse dilatation or ectasia of the œsophagus is that form of widening which occurs generally above a stenosis of the lumen, although it may occur when no stenosis is evident. It is generally fusiform, although the weight of the ingesta tends to make a considerable bulging toward the lower part of the sac; in the case of a stricture, spasmodic or organic, the greatest dilatation usually occurs immediately above the site. The majority of all ectasias are in the lower third of the tube.

**Etiology.**—Although sometimes found as a congenital lesion, an organic stricture of the cardia or other part of the tube is the most common cause; spasm of the cardia can undoubtedly give rise also to dilatation,

<sup>1</sup> Holub, *Ther. der Gegenwart*, September, 1906

<sup>2</sup> Tamerl, *Wien. klin. Woch.*, 1904, No. 29.



which is brought about by the pressure of the food, which is unable to make its way through the orifice. Many so-called idiopathic cases<sup>1</sup> have been described, upon the etiology of which it is idle to speculate; it is supposed in these cases, as well as in those which are secondary to stricture, that atony or degeneration of the muscle has occurred. In some of the cases of this class a marked hypertrophy of the muscle is found, but this is more likely to be a resultant and compensatory change than a primary condition. Fleiner, Strauss, and others consider that these dilatations are explained by a congenital defect in the enteromeres, and that this is combined with a cardiospasm of neurogenic origin. Those spindle-shaped ectasias which are widest at the middle are probably due to the muscular weakness being greatest at that part, but the shape as observed at autopsy is probably quite different from the shape that is assumed when food is passing down; at such a time it is likely that the most extreme dilatation exists in the lowest part of the ectasia. Beneke's<sup>2</sup> view is a sensible one, which is that the traction and bulging of the lowest part of the sac, when it contains food, pulls together the walls of the upper part of the undilated tube below, thus causing a kind of valve action at that point, which still further prevents the egress of the sac contents. The wall of the œsophagus in a dilatation is generally inflamed, and often ulcerated, which assists greatly in keeping up the causative spasm. With the use of the fluoroscope a constantly increasing frequency of dilatation as a result of spasm is observed, and "cardiospasm with secondary dilatation" is now a well-recognized occurrence.

**Symptoms.**—These are generally masked by those of the stricture which gives rise to the dilatation; there is difficulty in swallowing, fluids and soft foods being most easily taken; the saliva is increased; regurgitation of undigested food with mucus is common; when the dilatation contains food there is often pain in the sternal region, a sense of oppression, dyspnœa, and regurgitation of the contents of the sac; with decomposition of the ingesta, foul breath and a bad taste in the mouth are present. The sound may pass without difficulty, although sometimes it will be obstructed in so decided a way as to give rise to the supposition that an organic stricture exists, even in a spasmodic case; when it is in the dilatation, the excursion of its distal end is freer than usual. In ectasia, as in diverticulum, the sac may be emptied and the contents found to lack hydrochloric acid, pepsin, and rennin, or the tube cannot be inserted as far as the stomach. The frequency with which the wall of the sac becomes inflamed by the decomposition of food brings it about that there may be continual discomfort in the sternal region, even when there is no food present in the œsophagus. There may be actual pain, radiating from the region of the cardia along the rib margins, and regurgitation of the sac contents may occur even before the conclusion of the meal; or again, this may be deferred until the patient is asleep and lying upon the side.

<sup>1</sup> Pietrkowski, *Arch. f. Verdauungskrank.*, Band x, Heft 2. See also Lerche, *Amer. Jour. Med. Sci.*, 1907, cxxxiv.

<sup>2</sup> *Deuts. Aerzte-Zeitung*, June 15, 1901.



**Diagnosis.**—This depends upon careful observation of the symptoms and examination of the contents of the sac for the absence of stomach secretions; the use of the tube or sound may demonstrate the wide sac and the causative stenosis, and sometimes the spasm. When the condition is suspected, it can best be verified by the use of a bismuth mixture put into the œsophagus and viewed by the fluoroscope, although Kraus points out that in early cases even this, as a rule, fails. The conditions with which it is most likely to be confused are organic stenoses without dilatation and deep diverticula.

**Prognosis.**—Ectasia, if not extreme, is consistent with long life, although occasionally death is brought about by inanition, which should be considered rather as a result of the stricture than the dilatation. If the spasm be cured, a moderate degree of care in the selection of food, avoidance of coarse and cold foods, as a rule, and slowness in eating, will usually enable the patient to live comfortably. The prognosis in an uncomplicated case rests upon the completeness with which nutrition can be carried on. The presence of severe inflammation of the wall is a menace, in that the muscle may be affected and weakened and the dilatation thereby increase, but especially because ulceration may occur, which carries with it the danger of perforation.

**Treatment.**—In cases due to spasmodic or organic stricture the treatment of the primary condition dominates the case. Treatment of the dilatation is unsatisfactory. When it is recognized as arising from cardiospasm, combined with treatment of the spasm, electrization of the walls by a stomach-tube electrode has proved beneficial. Apart from the treatment of the organic stenosis or the spasm, it is often useful to wash out the sac every night, and so avoid the decomposition of its contents, and combat the inflammation by the use of silver nitrate solution (1 to 3 per cent.) or solution of boracic acid (2 to 3 per cent.). Atropin may be administered in the usual doses with good effect.

### DIVERTICULA OF THE ŒSOPHAGUS

**Etiology and Pathology.**—Diverticula of the œsophagus are pouches of the wall whose cavities connect with the lumen of the viscus; the sac may be connected with the organ by a narrow neck, or it may be funnel-shaped, in which case no neck, properly so-called, exists. Diverticula are classed as “pressure diverticula” when they are caused by pressure from within, and “traction diverticula” when the force is exerted from without. These two forms have nothing in common, save that both are dilatations of the œsophageal wall, yet custom has led to their being treated together. Their pathology is widely different, and pressure diverticula, which will be treated of first, are most frequently not œsophageal but pharyngeal diverticula. Of pressure diverticula, then, it may be said that they are at times congenital, but the majority are the result of disease in the œsophagus or in the surrounding structures. The congenital diverticula are usually due to defective fusion of the muscle coats of the two sides at the median line posteriorly, and when

lateral appear to result from a lack of complete obliteration of the branchial clefts. Most diverticula, however, are not of this nature, but result from disease in the œsophageal wall.

Pressure diverticula<sup>1</sup> are oftenest found high up on the *posterior* wall of the œsophagus at the point where pharynx and œsophagus meet, opposite the unyielding cricoid cartilage, but they may be found elsewhere, when they show a predilection for the natural narrowings of the tube. Their causation is doubtless due to the fact that the effect of pressure of the wall between a firm bolus of food and a hard organ externally (such as tracheal calcification, a calcified thyroid, or even, it is said, a calcareous artery) is to injure the tissues; they are deprived of physiological rest by the constant movements entailed in eating and drinking. When the œsophageal wall is thus weakened, the muscular and supportive tissues become insufficient and stretch easily; after each considerable distension the wall fails to contract to its proper degree, and the lumen of the tube remains a little wider at this point than normal, and each successive dilatation increases the size of the pouch. When the wall is weakened, a diverticulum is caused by a stretching of the muscle fibres and a separation of one from another; when an individual group of fibres breaks, or when this separation occurs, a hernial protrusion of the mucosa and submucosa through the gap follows; rarely these protrusions are still covered by an incomplete muscle layer, but even when this is not the case the thickened submucosa forms a wall that is at times as thick as the normal œsophagus. When they result from such a hernial protrusion, they often have a narrow, slit-like opening; notwithstanding this, they may attain a large size, when their liability to rupture constitutes a menace. The increase of intra-œsophageal pressure by the passage of food distends yet more the beginning sac, and because of their production thus by pressure from within, these are called "pressure or pulsion diverticula." They occur most frequently in the male sex, and in middle or advanced life; it is supposed by some that pressure diverticula in the continuity of the tube are really the final result of traction diverticula; if this be true, these would be properly called "pressure traction diverticula," a class described by some authors.

The "traction diverticula" are produced in quite a different way from that already described; some nearby structure, such as a lymph node, gains adhesion by inflammation to the outside of the tube, and the contraction of the inflammatory tissue during the process of fibrosis or scar formation makes a constant traction on the wall, which is pulled out at this point. A high intra-œsophageal pressure during the passage of food assists this process, and a small, frequently funnel-shaped diverticulum results. Since the lymph nodes at the tracheal bifurcation are oftenest the cause of this form of diverticulum, it is most frequently found at this level on the *anterior* wall. Tuberculosis, extremely common in these nodes, is a frequent excitant; Zenker and Heller have pointed out their liability to inflammation secondary to pericarditis; caries of the spine has also caused it.

<sup>1</sup> See Richold, *Deuts. Archiv f. klin. Med.*, 1904, lxxx.

Schmorl found traction diverticula in 3.5 per cent. of all autopsies<sup>1</sup> (a figure which appears excessive), and one-third of these had led to perforation into surrounding tissues, under which circumstances they may lead to infiltration and subsequent gangrene of the lungs, rupture of a bloodvessel, or some such accident. These diverticula appear so insignificant on the œsophageal wall that one cannot at first understand that they are liable to perforation; yet one in our own series appeared to be only 2 or 3 mm. deep, but a fine probe inserted passed up what looked like a fibrous cord, fully a centimeter to the peritracheal node situated on the outside. In this narrow passage a small piece of solid material, such as a seed, might readily become caught, and the funnel shape of the diverticulum tends to allow any such foreign body to pass up into the narrow channel beyond. Once lodged here, it could ulcerate its way out. It may be said that the question of the origin of diverticula of the œsophagus has occupied attention far beyond its merits and the volume of controversial literature on the subject is very large.

**Symptoms.**—Traction diverticula, from their small size, give no symptoms and are rarely discovered during life, and then only by œsophagoscopic or fluoroscopic examination. Pressure diverticula of the œsophagus, if small, give no symptoms and are frequently not recognized. If, however, a diverticulum be large, and be filled by liquid or food material, the decomposition of this and the irritation produced thereby will give rise to vomiting; the patient may feel a sensation of "something in the throat;" there often is difficulty in swallowing, which is greater when the diverticulum is full, so that it compresses the œsophagus proper. Under such circumstances respiration may be interfered with and the neck may be larger than usual, or an actual tumor appear. Pain is rarely present, unless ulceration of the diverticulum exists; it must be remembered that even a small diverticulum may become the seat of ulceration by lodgment of a seed or small, hard food particle.

From the decomposition of its contents foul breath arises, and the inflammation so set up may spread to the œsophagus itself, or may even proceed to ulceration and rupture, with the formation of peri-œsophageal abscess; or the break may occur into the thoracic cavity, setting up gangrene of the lung or empyema; a diverticulum has been known to burst into a tuberculous cavity of the lung. When the diverticulum is small the tube will readily pass it, but as it becomes larger the tube is often directed into the sac itself, where the mobility of its lower end and the impossibility of passing it farther may assist the diagnosis. The tube is especially liable to pass into the sac if the latter is full, thereby pushing the œsophagus forward out of the direct line and taking its place.

**Diagnosis.**—This may be made occasionally by palpation if the diverticulum be sufficiently high to appear in the neck; if filled with air it will be tympanitic, if with fluid, dull on percussion, and external pressure will sometimes succeed in emptying it. Cooper<sup>2</sup> states that a succussion splash may be heard in certain patients, and advises that in

<sup>1</sup> Riebold, *Deut. Archiv f. klin. Med.*, 1904, lxxx, Heft 5 und 6.

<sup>2</sup> *Jour. Amer. Med. Assoc.*, 1910, lv, p. 856.



the morning, when the diverticulum may be empty, as much water as possible be drunk: the neck is then seized and shaken. A diverticulum situated high up will rarely become completely full, for the act of swallowing tends to empty it. If lower down, the failure to find hydrochloric acid in the regurgitated material may indicate that it does not come from the stomach, and the stomach tube may succeed in reaching fluid at so high a level that it could not be in the stomach; if the tube can be passed with certainty into the diverticulum, which is often a matter of much difficulty, a mixture of carbonate of bismuth and syrup of acacia can be introduced, which will render the diverticulum opaque to the *x*-rays. It must always be borne in mind that the sac is easy to perforate. The diagnosis has been made by recognizing food which has been eaten several meals previously, when the stomach has previously regurgitated food more lately taken. However, unless one or other of these accidental circumstances gives a clue, the recognition of diverticulum is very difficult in the absence of fluoroscopic examination. In a recent case under my own observation, the patient had a spasmodic stricture, sometimes only momentary. Under examination by *x*-rays, a diverticulum appeared which filled during the brief period of spasm, and instantly emptied as the spasm relaxed.

**Treatment.**—Diverticula large enough to be recognized demand treatment, although this is not very easy. Feeding by the tube, when it is possible to pass it by the orifice of the diverticulum, is advisable, and if the shape of the sac be determined, and the neck of it found to admit the procedure, surgical removal should be advised. This as yet applies only to those situated in the neck, but the surgical methods of differential pressure for intrathoracic work, now so extensively used, extend the possibilities of operation. In the event of a diverticulum being recognized, and the advent of ulceration observed, *e. g.*, by the presence of blood in the contents, rectal feeding or gastrostomy will be necessary for a time because of the danger of rupture. While erosions are healing, potassium bromide, ʒij (gm. viij), or morphine, gr.  $\frac{1}{2}$  (gm. 0.03), daily, may be used to lessen irritability, although physiological rest by withholding food is the most rational procedure. Regular washing with water greatly assists the patient by the prevention of decomposition, thus lessening inflammation, and by increasing the tone of the muscle. At intervals of a few days, a solution of silver nitrate (1 per cent.) may be used, and the washing of the sac can be taught to an intelligent patient. When cardiospasm is present, the occasional passage of a large bougie will assist in overcoming it, but this procedure should always be done by the physician, and never by the patient. Electrolysis is widely used by employing a gastric electrode inside the sac. The most important requirement is a well-regulated, rich diet; fats, butter, and oils are desirable, and when ordinary feeding is practised, one or two teaspoonfuls of melted butter or olive oil are recommended to be taken a little before food time, to act as a lubricant. Many patients are able to empty the sac by certain gymnastics, such as the motions of rowing; it is obvious that, apart from washing, a sac can scarcely be kept clean by such measures alone.



### STENOSIS AND STRICTURE OF THE ŒSOPHAGUS OF NON-MALIGNANT ORIGIN

Obstruction of this nature, apart from benign tumors, to be spoken of later, may be congenital or acquired; the latter may be spasmodic or organic (fibrous). The spasmodic variety has been already dealt with as a neurosis.

**Etiology.**—A congenital stenosis has been undoubtedly found in a number of cases with no trace of fibrosis; it is generally in the upper part of the œsophagus, annular or fusiform in shape, and concerns the mucosa and submucosa only. A case is described by Mayer which underwent cure. The condition is an extremely rare one, and before deciding that a stenosis is congenital the history should be carefully searched for even a slight trauma.

The fibrous stenoses take origin in any inflammation, wound, corrosion, burn, or ulceration in which the loss of substance is so great that a considerable amount of fibrosis replaces it. In a general sense it follows that the greater the loss of substance, the more certainly will a serious degree of stenosis occur, and the greater the length of surface implicated in the original lesion, the greater will be the longitudinal extent of the stenosis. In the case of corrosives, the more concentrated they are, the greater likelihood there will be of a rapidly ensuing stricture, while much diluted corrosives are apt to form more slowly developing and less complete stenoses. Thus it follows that with a very severe corrosion the patient will probably never be free from dysphagia until the stricture is formed, whereas the lesser grades of corrosion may seem to heal, and after a period of normal patency one finds with disappointment that the sequela of the corrosion has to be reckoned with, months later, in the guise of a slow stenosis. The sites where stricture is most likely to occur are the natural narrowings, *i. e.*, at the cricoid, the tracheal bifurcation, and the diaphragm, yet definitely annular stenoses are at times found elsewhere. The peculiar liability of these parts is due to the momentary delay of the corrosive or burning material at those points. The entire œsophagus has been stenosed in certain cases. When the stenosis is once established a moderate degree of dilatation is often to be observed above it. (See Plate VII, Fig. 1.)

**Sequelæ.**—In cases of stenosis, inflammation, either due to the injury which caused the stenosis or as a secondary result of it, may spread to the surrounding structures, or may lead to perforation. A possible sequel is injury or even perforation by the sound, especially when dilatation or pouching of the œsophagus above allows the sound to stray from the lumen.

**Symptoms.**—The invariable sign of stenosis is difficulty in swallowing, which is constant, generally progressive, and fluids are more easily taken than solids. Pain is generally absent. The food that does not pass through is regurgitated after a variable time; the presence of a dilatation above the stricture is likely to be accompanied by delay in the regurgitation. The patient generally knows his capacity for swallowing liquids

## PLATE VII

FIG. 1



FIG. 2



FIG. 3



Fig. 1.—Stenosis of lower half of œsophagus of a child, resulting from drinking lye. Dilatation of gullet above the stenosis.

Fig. 2.—Epithelioma of œsophagus. A flat, shallow, ulcerated growth is seen spreading over a relatively large surface.

Fig. 3.—Epithelioma of œsophagus. The upper part of the growth is flat, the lower much more nodular. The stomach wall is partly cut away to show a lymph node with great secondary involvement.

(From specimens in McGill Medical Museum.)



at any time, and will, in partial stenoses, not exceed the amount that can pass down; the food or drink is felt to "stick" at a certain point, referable generally to the top of the sternum. The point of stenosis can be determined accurately by the tube or sound, although a second lower stenosis may exist; when the site of the stenosis is determined, graduated sounds should be used, beginning with the large and proceeding to the smaller ones, until one is found which can enter the stricture. It is to be remembered that the existence of the stenosis tends to excite spasm, and this at first may make the stenosis appear more extreme than it really is. If the stenosis is at all considerable, the auscultatory sounds can be recognized as ceasing at the affected level. In the absence of treatment, any degree of stenosis will be attended with loss of weight from malnutrition, because the mental anxiety attendant on the dysphagia tends to keep the patient from using his œsophagus even up to its limited capacity.

**Diagnosis.**—This must be made between this condition and stenosis from carcinoma or from spasm; foreign bodies (which have been known to remain in the œsophagus for astonishingly long periods); polyps and external tumors pressing on the œsophagus must also be considered. The history of injury is of the highest value. In any case, before proceeding to the examination, one must be reasonably sure that aneurism does not exist; then one must consider carcinoma, because it is the most frequent and likely cause; its rapid progress and the greater degree of emaciation, with absence of a definite trauma, are all useful indications. The *x*-rays will frequently determine if a foreign body be present; the benign tumors, such as polyp, are rare, but they may be impossible to differentiate, save by the non-progressive nature of the lesion.

**Prognosis.**—This cannot be given in so many words, but depends upon the degree to which nutrition can be kept up and the certainty with which aspiration of food into the respiratory tract can be avoided. The earlier the stage at which treatment is begun, and the more youthful the patient, the better is the prognosis for cure.

**Treatment.**—This is palliative and curative, and the latter should always be tried. Many surgical procedures have been advised which depend for their reasonableness upon the site of the obstruction; excision of the stricture, internal and external œsophagostomy, even the cutting of the stenosis by fishing-line, have all been, at times, successful. Rapid dilatation is dangerous, but in cases of cardiac stenosis gastrostomy followed by dilatation from the stomach is rational. Considered broadly, the best treatment is gradual dilatation; as was stated during the consideration of spasm of the œsophagus, there are various means of accomplishing this: a thread may be swallowed, upon which a wire is run, and on this, in turn, bulbs or olives of varying size are projected: or rubber bags distended by fluid may be used; or, as is probably most likely in the case of the physician, the old-fashioned sound may be the means available. This last consists in the passage of the largest sound that will pass, every other day for several times, then using the next largest similarly for a time; the sound should be left in for ten or more minutes at each treatment. In this way the stricture will sometimes yield com-



pletely, after which it is well to pass a large sound at rare intervals to be warned of a recurrence and to prevent it. If nutrition is failing, gastrostomy should be done, even while the treatment is in progress, or before it is begun. A most important fact is that careless use of the sound may irritate the surface and add to the stimulus already producing the fibrosis, while the danger of perforation, especially when there is dilatation of the gullet above the stenosis, must always be remembered. Fortunately, the stenosis is generally funnel-shaped, and, therefore, the sound is insensibly guided in the right direction. The bloodless nature of the operation does not render it unworthy of the best surgical skill that can be obtained. Ingenious operations devised for the construction of a new gullet from portions of the stomach or even from the skin have not proved their feasibility.

A number of case reports, chiefly from German sources, speak favorably of the employment in organic stricture of thiosinamine (allyl sulphocarbamide); repeated injections are made hypodermically of gr. j to ij (gm. 0.06 to 0.12) every two or three days, and the result is said to be softening of the stricture to such an extent that where bougies could not be passed they were readily admitted after a few administrations. Zuberbühler<sup>1</sup> advises electrolysis, the kathode being placed upon the stricture, and a current of 5 to 20 ma. used for five minutes at a time.

Palliative treatment includes such measures as gastrostomy and the wearing of a permanent tube to allow of passage of fluids through the structure; the latter device is especially useful, as it eliminates the spasmodic increase of the stenosis. As a palliative measure, œsophagotomy is not as simple as gastrostomy, and is probably not preferable.

### CARCINOMA OF THE ŒSOPHAGUS

The most important disease of the œsophagus is cancer, which commands attention by reason of the readiness with which the narrow lumen of the organ is obstructed, as well as by the importance of the neighboring structures which are likely to be infiltrated. So frequent is the occurrence of carcinoma that we may say that in every patient between the ages of forty and seventy years, with a stenosis of the œsophagus without other evident cause, the odds are overwhelmingly great that it is due to carcinoma.

Cancer of the œsophagus is surpassed in frequency of occurrence only by cancer of the uterus, female breast, and the stomach. Figures, as usual, are conflicting; our Montreal series of 5480 autopsies shows 29 cases of œsophageal carcinoma, a percentage of 0.53. Kraus<sup>2</sup> gives figures which aggregate 216 cases out of 45,405 autopsies, a percentage of less than 0.5; but as some of these series date back as far as 1830, it is possible that certain cases may have been overlooked. The Russian statistics show an astonishing frequency of the disease, one series indicating that the œsophagus was the seat in more than 32 per cent. of all

<sup>1</sup> *Berl. klin. Woch.*, 1908, xlv, p. 16.

<sup>2</sup> Kraus, *Die Erkrankungen der Speiseröhre*, Wien, 1903 (Nothnagel's *System*).

carcinoma cases; a series of 981 cases of carcinoma, compiled from Kraus, gives a percentage of 20 for the œsophagus, but this contains three series of Russian cases. Our series at the Montreal General and Royal Victoria Hospitals, in 3882 cases, gave 265 carcinomas, 24 of which were of the œsophagus, *i. e.*, 9 per cent. In this series it is surpassed in frequency by carcinoma of the stomach, female breast, and of the colon; into this list, ordinarily, would come the uterus, although, as usually happens in General Hospitals, autopsy figures in regard to carcinoma of the uterus are very low. In using autopsy figures it must be remembered that the breast and uterus, which are comparatively accessible and admit of surgical treatment, show a frequency of occurrence far below their real position. In 38,000 hospital entries at the Royal Victoria Hospital, Montreal, there were 53 cases of carcinoma of the œsophagus.

**Etiology.**—Carcinoma of the œsophagus is a disease of middle or advanced life, being found most frequently between the ages of fifty and sixty years; the earliest case of which a record was found was at nineteen years; one case in our own series occurred in a woman aged thirty-two years. The male is much more liable than the female sex, the largest series showing a ratio of 3 to 1. Smaller series show as great a preponderance as 7 to 1.

Our knowledge of the causative factors of this disease, as in carcinoma elsewhere, is very small; irritation has been considered as of more moment than any other contributing cause, and alcoholics are considered as especially liable. Stress is laid upon the occurrence at the physiological narrowings, and upon the histories frequently given by patients in whom the first symptoms followed the swallowing of a mouthful of hard food or of hot material. The arguments in favor of trauma as yet appear insufficient. It is also to be pointed out that carcinoma not infrequently seems to spring from scars of the œsophagus, from traction diverticula, and from the walls of dilatations; but this, as well as its occurrence in drinkers, is probably but another way of saying that chronic inflammatory conditions predispose to its occurrence. Paul Wolf<sup>1</sup> cites three cases, to which Schmorl adds two, in which carcinoma of the œsophagus developed at the site of a spondylitic deformity of the vertebræ. He points out that it may be that the vertebral deformity caused a bend in the œsophagus at this point, so that irritation caused by the passage of food was added.

**Special Pathology.**—Carcinoma of the œsophagus is nearly always primary, and its most common mode of occurrence as a secondary growth is when it spreads by extension from a growth of the cardiac end of the stomach, or less frequently from the thyroid gland, in which cases the growth is of the same nature as the original neoplasm.

The tumors vary much in appearance and extent, perhaps because one sees them at autopsy in so widely different stages. By reason of the organ involved, death frequently occurs from intercurrent disease or accident; thus it happens that often one is enabled to see a growth not long after its commencement. At times the carcinoma appears as

<sup>1</sup> *Münch. med. Woch.*, 1903, No. 18.

an isolated mass on one wall, oftenest the anterior; at other times a flat growth spreads over a relatively great area (Plate VI, Fig. 2). Gray or white or yellowish white in color, it often shows little scattered islets extending from the periphery of the main growth; very frequently the growth is annular, encircling the tube (Plate VI, Fig. 3). Again, a section through the stenosis will show a yellowish-white thickening of the wall of the gullet with comparatively slight evidence of nodular growth on the mucosal surface; or again, one finds a large, soft, irregular, cauliflower-like, fungating mass that seems to more than fill the lumen of the œsophagus, whose ulcerated surfaces bear witness to the difficulty with which patency of the tube has been maintained. As a rule, not more than one or two inches of the tube are implicated, but cases have been known to affect the entire length of the organ. All degrees of hardness are found, but generally the mass is soft; a real scirrhus carcinoma has not come under personal observation. Degenerations are the rule, and necrosis of large parts of the tumor is very commonly seen. One is frequently struck by the fact that the tumor mass seems inconsiderable in comparison with the symptoms to which it gives rise.

The degree of stenosis depends on the size and the consistence of the growth plus the possible spasmodic stenosis set up by its presence. By the lodgement of food and the weakening of the walls a dilatation is often formed above the stenosis. Variations in the degree of stenosis occur, so that the occurrence of ulceration and the detachment of pieces may be the signal for the subsequent easier passage of food. Ulceration in the main growth is almost sure to occur from the attrition of the apposing walls of the gullet, and from the passage of food; the irregularity of the growth makes many small hollows and bays, in which decomposition is likely to be set up and the ulceration thereby hastened. Strangely enough serious hemorrhage from such ulcerations is rare, and the amount of blood is small; pieces of the growth which are detached either are regurgitated or pass into the stomach and are digested.

Histologically, most œsophageal carcinomas are squamous-celled (epitheliomata), although adenocarcinomas are found in a certain number of cases, taking origin from the glands scattered throughout the organ. Of the former class, many are properly basal-celled carcinomas: perhaps one might say that all of the squamous-celled carcinomas exhibit somewhere in their structure the basal-celled quality. The growth is frequently seen arranged in the familiar circular masses, and true epithelial "pearls" are generally to be observed; various differences are seen in the amount of fibrous stroma that exists, and the more fibrous stroma there is, the less is the malignancy of the growth, or perhaps it is better stated that the more fibrous stroma there is, the less rapid is the progression of the growth. Mucoid degeneration has been described, and a single report of primary carcinoma myxomatodes is to hand (O. Fischer<sup>1</sup>).

**Site.**—The commonest site has been a matter of endless debate and is very difficult to designate. The level of the bifurcation of the trachea seems to be affected oftener than any other place, and as to which third

<sup>1</sup> *Prag. med. Woch.*, 1899, xxiv, pp. 30, 31.



of the gullet is the most liable to carcinoma, a study of the literature indicates the lowest third; but this statement is made without conviction; it does not greatly matter, for it is a well-proved fact that no part enjoys any exemption. A favorite text-book statement is that the points of physiological narrowing are more liable to be attacked than are other parts, but this statement loses value when one finds that, according to Kraus, thirteen different points of narrowing have been described in the 25 cm. length of the tube. It does seem possible to state, however, that a very small fraction, perhaps a tenth of all growths, lie in the neck, where they are readily accessible.

**Perforation.**—This is surprisingly frequent; in Petri's series of 44 cases, 27 perforated. The perforation may occur into different organs or areas, depending upon the site of the growth, but in by far the greatest number the ulceration is into the larger air passages, the larynx, trachea, or a bronchus; apart from these, into the mediastinal tissue, the pleura, the lung, or even, although a rarity, into the pericardium. Perforation is not of itself necessarily fatal, but death follows soon, as a rule, because the œsophageal contents set up aspiration pneumonia or gangrene. When the rupture occurs into the mediastinum, interstitial emphysema of the tissues of the neck may be seen, followed by cellulitis. When the pleura is densely adherent to the lung, the lung tissue itself may be directly invaded by the material escaping from the opening. Occasionally the perforation occurs into a bloodvessel.

**Extension to Neighboring Structures.**—Many different structures may be invaded and damaged by the extension of the growth, chief among which are nearby arteries, the vagus or the sympathetic nerves, the recurrent laryngeal nerve, if the growth be left-sided, or even the thoracic duct and the brachial plexus. The vertebræ have been eroded, and an œsophageal carcinoma has been known to produce pressure on the spinal cord. In the case of the veins, the gradual pressure of the invading neoplasm leads to a thrombosis, so that by the time the wall is eroded the danger of hemorrhage is obviated. In the arteries, on the other hand, there may be no such protection, and fatal hemorrhage has occurred in a number of cases. Most of the important arteries near the œsophagus have been implicated by extension of œsophageal cancer; the carotids, the subclavians, the intercostal and vertebral arteries have been invaded, and of 50 cases of arterial implication collected by Knaut, 32 occurred in the thoracic aorta. Those cases in which the heart, generally the auricles, has been attacked by the growth, where particles have been broken off and carried to other parts of the body, are to be regarded rather as curiosities than as actual clinical probabilities. A growth at the cardiac end is very apt to spread to the peritoneum or into the diaphragm.

For many years an impression prevailed that carcinoma of the œsophagus had not so great a tendency to form metastases as had carcinomas elsewhere, but this arises from no inherent peculiarity of the growth itself; it possibly happened that the secondary growths in the deep cervical glands were often overlooked; it is even more likely that the importance of the structures involved leads to a comparatively early



fatal result, at which time the lymphatic involvement, and especially extensive involvement of distant organs, is as yet not prominent. The comparatively short duration of carcinoma of the œsophagus is in favor of this explanation. Twelve cases at autopsy in the Royal Victoria series showed secondary growths in eight.

**Symptoms.**—In the majority of cases the earliest symptom is a difficulty in swallowing, which at first occurs only with a hard or dry mouthful of food, with a feeling of discomfort at the site of the growth; as the patient describes it, there is “something there.” A mouthful of fluid generally suffices at first to wash down the obstructed mass. In one case of our own series the stenosis at death was so great that the circumference of the gullet at the growth was 1.5 cm., yet the patient, having been living on fluids, never complained of dysphagia. The progress of the difficulty in swallowing is at times slow, but is constant; an exception to this is that sometimes late in the disease a piece of the growth may be broken away and the lumen widened. At first, merely hard pieces of food give difficulty or discomfort, then there is obstruction to soft foods, and finally to fluids, so that ultimately none, or at best, very little fluid can be taken. Attempts at swallowing excite cough, and frequently regurgitation occurs, which may be immediately after the food is taken, or delayed for hours. The higher up the stenosis, the more prompt is the regurgitation, and the lower, the longer delayed. Regurgitation of food is frequently preceded by severe retching, and the regurgitated food is generally alkaline, mixed with much mucus, and shows no peptonization. If the growth be ulcerated, the regurgitated material may be mixed with blood, and particles of the growth may be found; under these circumstances the breath is usually fetid.

Commonly, discomfort or a feeling of oppression is felt under the sternum, localized to the site of the growth, although severe pain may be complained of; it is at times referred to the xiphoid region, instead of to the actual situation of the growth. The severe pains are of a tearing or piercing character, at times radiating widely to the back, neck, or shoulders. Such pains are often nocturnal, and may be independent of attempts to take food; although pain is, in most cases, a late symptom, it must not be forgotten that it may be the earliest indication of the disease, preceding even the difficulty in swallowing. Guarnaccia<sup>1</sup> states that in all cancers of the upper third of the œsophagus, even in the early stage there is a progressive fixation of the tongue, so that it can be protruded only with difficulty and pain, and that it becomes almost impossible for the observer to draw it out.

With the gradual increase in the difficulty of taking food there is great weakness; the loss of flesh is rapid, and may be extreme, while many patients complain of severe thirst, less frequently of hunger. The cervical and supraclavicular lymph nodes, when involved by secondary growth, are enlarged and at times palpable, especially on the left side. It is scarcely necessary to give in detail the symptoms that arise from pressure upon the various nerves which may be implicated. It is said

<sup>1</sup> *Arch. Int. de Laryng.*, 1912, xxxix, p. 88.

that in as many as a sixth of all cases there is a contraction of the corresponding pupil, with ptosis, falling in of the bulbus, and sluggish reaction to light (Hitzig); these pupillary changes are most often seen on the left side, and depend upon pressure on the sympathetic nerves; there need not be with it a paralysis of structures supplied by the recurrent laryngeal. The so-called Horner's complex—ptosis, miosis and enophthalmos—is occasionally noted as present. The involvement of the sympathetic means that lymph nodes have implicated the nerves, and does not tell the site in the œsophagus; especially is involvement of the right recurrent apt to be by lymph nodes, because on the left side the nerve lies so close that the primary tumor may affect it. When the recurrences are involved, there may be a very serious dyspnœa, which may come on even before dysphagia has become prominent. More common than any other single sign, probably, is paresis or paralysis of the vocal cords from interference with the recurrent laryngeal nerve.

If no contra-indication exists (the presence of aneurism should always be excluded), a local examination by the use of the tube and bougies will determine if an obstruction really exists and its exact position. If bleeding is excited by the use of the tube, the further examination by bougies should be postponed, but should no such contra-indication exist, one can sometimes determine, by using bougies of diminishing calibre, at what level in the growth the stenosis exists, and may even guess at its extent. The greatest care should be used in passing the bougie to avoid perforating the wall, an occurrence by no means infrequent in careless hands. When using the tube, the contents of the eye of the tube should be noted, as pus, blood, or mucus may be found; more rarely, particles of the growth are obtained. The examination of the contents of the stomach is not of moment, for normal acidity, hyperacidity or anacidity may exist.

Of great value, but of some difficulty of application, is the use of the œsophagoscope, by which the growth can be actually seen, and its nature and extent, at least as far as the stenosis, be accurately determined. The x-rays may enable a correct diagnosis to be made. Reference has been made to the zig-zag course sometimes taken by the narrowed lumen.

**Diagnosis.**—This is well summed up as follows: "If there is steady loss of flesh, with increasing dysphagia, in a middle-aged or elderly person, suspect carcinoma; if the sound is arrested, the diagnosis is very probable; if there is slight bleeding with the use of the sound, it is all but certain." In its early stages the disease may be confounded with almost any œsophageal disease; it may preserve its likeness to benign stricture for a considerable time; an advanced case is generally recognized without difficulty. It is obvious how useful œsophagoscopy examination by a trained eye may be in an early case.

**Prognosis.**—The duration of the disease varies between six months and two years from the appearance of the first symptoms, although at times its entire course is measured in weeks. In 104 cases, Lamy<sup>1</sup> states

<sup>1</sup> *Arch. des. Mal. de l'App. Digest.*, Paris, August, 1910, iv, No. 8.

that the majority succumbed in less than twelve months. The prognosis is very bad; carcinoma of the œsophagus in an accessible part is but a small proportion of the whole, and even in these surgical treatment must admit a large mortality and a small percentage of cures.

**Treatment.**—This is in most cases palliative, but in a few may be curative. The few cases in which the growth is early and accessible offer chances of success under surgical treatment, and even the intrathoracic growths are now being attempted. In all cases other than the above the treatment can be only palliative; the principles of such treatment are simple, keep up the nutrition, feed by the mouth as long as is possible, counsel an œsophagostomy or gastrostomy, preferably the latter, when mouth-feeding is impossible or about to become so, and keep the patient as free as may be from pain.

The preservation of nutrition is the most important factor, although difficult of accomplishment. Good judgment and the utilization of the patient's experience are requisite in the selection of articles of diet. The stringy mucus which so often troubles the patient is lessened by the use of solutions of sodium bicarbonate (1 to 10) as a wash for the mouth, or to be swallowed. A demulcent quality in the food is desirable. Liebermeister<sup>1</sup> states that when the œsophagus is obstructed by carcinoma, ease in swallowing may be obtained by the patient sipping a small quantity of 1 or 2 per cent. hydrogen dioxide solution. It may be necessary to give morphine or atropine hypodermically before each meal.

Many physicians practise intubation of the stricture, for which various procedures have been devised. One of these is a tube, of which the upper end is fixed in the back of the mouth (by cords fastened around the ear or in other ways); it passes through the stricture to the stomach. Another method is the use of a short tube, with a projecting rim which rests on the stricture, which passes the narrowing. It is placed in position by a whalebone guide, and is also secured above by cords through the mouth. Care of the cords is necessary. If a fistula into the respiratory tract has occurred, the use of a tube is essential to the continuance of mouth-feeding, and at this point it may be stated that most clinicians are of the opinion that it is necessary to carry on mouth-feeding as long as possible, to utilize, for one thing, to the full degree, the salivary secretions and their admixture with the food.

With the gradual increase of stenosis further means need to be undertaken, lest the patient die rapidly from starvation; œsophagostomy below the stricture or gastrostomy is indicated, but for various reasons gastrostomy is the operation generally preferred. It is a difficult matter to counsel a gastrostomy at the right time; it is almost certain to be required, and if delayed too long the patient is apt to die from the effects of the operation, or the degree of starvation is so great that its good effects are not realized. On the other hand, the patient will often object to the operation so long as the œsophagus remains moderately patent. No rule can be laid down for a decision; a frank explanation of the circumstances to the patient and the patient's friends should be made.

<sup>1</sup> Liebermeister, *Münch. med. Woch.*, September 19, 1911, lviii, No. 38.



If pain be severe, it should be treated. The application of a few drops of weak silver nitrate solution (1 or 2 per cent.), or 10 to 15 drops of a 3 to 4 per cent. solution of eucaine, or 10 drops of a 1 per cent. solution of heroin, repeated thrice a day, will be found to relieve pain; if these prove inefficient, the hypodermic injection of morphine is the most satisfactory method. Ten drops of a 1 per cent. solution of the extract of *nux vomica*, taken thrice daily, is recommended; the astringent solutions of silver nitrate will at least assist cleanliness.

The external use of the x-rays has not been of service, but Einhorn<sup>1</sup> reports benefit in retardation of the growth from the use of a radium vial in a hard-rubber capsule, which is screwed into the end of a flexible rubber tube and left in position for one-half to one hour at a time.

*Sarcoma* of the œsophagus occurs rarely, but 24 cases have been collected by Hacker.<sup>2</sup> Three-quarters of these were in males, and more than three-quarters in the thoracic part of the gullet. Metastasis was frequent. It cannot be differentiated during life from carcinoma, save by the microscopic examination of fragments of the growth. Its treatment is identical with that of the commoner neoplasm.

### NON-MALIGNANT GROWTHS OF THE ŒSOPHAGUS

Non-malignant new-growths of the œsophagus deserve only brief mention. The commonest is fibroma, or fibrous polyp, which not infrequently is pharyngeal in origin, and as it grows hangs down into the œsophagus. Rokitansky reported one seven and a half inches in length and two and a half inches in thickness. An interesting case (Monro), coming from the Edinburgh Hospital in 1763, appeared in the Edinburgh Physical and Literary Essays of that time. By movements of vomiting and coughing it could be projected to the front teeth, but had to be swallowed almost immediately to prevent choking. A ligature was tied around it, it was reswallowed, and allowed to slough, the piece coming away *per anum*. Two years later it caused death.

These growths may be sessile or pedunculated, the former being probably the earlier stage; they are elastic, firm, and are apt to be ulcerated; although generally single, they may be multiple. Myomata, fibromyomata, and lipomata<sup>3</sup> also occur; finally, more frequently than any of the last named, are those proliferations of mucosa and submucosa called papillomata, which are pedunculated, soft, and often multiple. They rarely give rise to symptoms of any degree of severity. All the signs of new-growth may fail with these neoplasms, provided they be not large enough to cause difficulty in swallowing, but if they are large, one may find, as in carcinoma, pain in the chest, radiating to the back and epigastrium, becoming accentuated on swallowing, especially if ulceration be present; the differential diagnosis rests upon the preservation of nutrition if actual sight of the tumor by the œsophagoscope is not possible. Surgical treatment may become necessary.

<sup>1</sup> *Jour. Amer. Med. Assoc.*, July 1, 1905, xlv.

<sup>2</sup> *Milth. a. d. Grenzgeb. d. Med. u. Chir.*, Band xix, Heft. 3.

<sup>3</sup> See Glinski, *Virchows Archiv*, 1902, Band 167.



## CHAPTER IV

### FUNCTIONAL DISEASES OF THE STOMACH

By JULIUS FRIEDENWALD, M.D.

#### GASTRIC NEUROSES

**Introduction.**—Gastric neuroses are those functional disturbances of the stomach manifesting symptoms of a nervous character and not based upon any anatomical pathological changes. A certain number of the so-called gastric neuroses, dependent without question upon some form of anatomical change, have up to the present time eluded our means of detection. With more and more exact methods of investigation, the number of gastric neuroses will gradually be lessened in number, and some of these diseases be placed upon a more definite anatomical basis.

It is now but little understood in what manner the disturbances of innervation take place; it is well known, however, that the branches of the vagus and abdominal sympathetic carry the impulses to and from the stomach, and it is through these nerves that these disturbances of innervation occur; while we cannot trace the exact paths, it is generally believed that the impulses of motility, sensation, and secretion are transmitted by different nerves; since any of these disturbances may exist alone and independently of the other, we therefore believe in the existence of special nerves of motion, secretion, and sensation.

It will not be out of place to briefly discuss a few points associated with the nervous mechanism of the stomach. Between the circular and longitudinal muscles there is a plexus of nerves (Auerbach's plexus) by means of which a local nervous mechanism is maintained. Intimate connection with the great nerve centres is had through the vagi, while in addition to these the sympathetic sends fibres to the stomach. It has not yet been entirely determined whether the rhythmic contractions of the stomach and intestines are entirely under nervous control, since this special process is regarded by some as being of muscular origin alone. Magnus<sup>1</sup> considered these contractions of nervous origin. He succeeded in obtaining rhythmic movements of the muscles of the intestines taken from the body which still held the plexus of Auerbach, even after the removal of the plexus of Meissner and the mucosa.

Through the researches of Langley, H. Meyer and Gaskell, much attention has been recently attracted to the functions of the vegetative or autonomic nervous system, which includes all of the efferent nerve fibres (outside of the cerebrospinal axis), excepting those supplying the voluntary muscles. There are two groups of fibres of the autonomic nervous system, which must be distinguished from each other.

<sup>1</sup> *Die gesammte Physiologie*, 1904, cii, 362.

The first group, includes those fibres taking their exit from the thoracic and lumbar region of the spinal cord, and known as the sympathetic proper, which supply the bloodvessels, glands and smooth muscle fibres of the entire body, including those of the stomach and intestines, bile and pancreatic ducts, liver and pancreas, colon, sigmoid and rectum.

The second group or autonomic proper (non-sympathetic), includes the nerves taking their exit from the mid-brain; hind-brain, and sacrum, supplying the glands and muscles of the gastro-intestinal tract, the œsophagus, stomach, intestines, liver, biliary passages, pancreas and ducts, colon, sigmoid and rectum. This group has been termed cranial-sacral autonomic system, or "the vagus system in the larger sense."

Through the researches of Eppinger and Hess, the theory has been advanced that disturbances of the autonomic system leading to increased and decreased tonus or excitability, may be the cause of certain pathological changes, and that through this system, the activity of the glands of internal secretion are controlled and regulated. According to this theory the symptoms of nervous dyspepsia are due to disturbances of internal secretion in consequence of which increased or decreased excitability or increased or decreased tonus is transmitted by way of the autonomic system to the stomach and intestines.

Eppinger and Hess have according to this plan evolved a clinical symptom-complex, which is based on the excitability or tonus of the autonomic system, and is termed by them vagotonus, and sympathetico-tonus. The effect of the increased tonus of the craniosacral system controlling the digestive organs consists in an increase in secretion of the stomach glands (hypersecretion and hyperacidity), increased gastric peristalsis (nervous vomiting), cardiospasm, pylorospasm, spastic constipation; increased intestinal peristalsis (nervous diarrhœa), mucous colitis, and spasm of the rectal sphincter.

As forms of increased sympatheticotonus, may be mentioned, atony of the stomach, ptosis, atony of the intestines with increased constipation, achylia gastrica, nervous anacidity and relaxation of the anal sphincter.

It is still doubtful whether or not the pylorus is partially under local nervous control, for Cannon<sup>1</sup> has shown that destruction of either of the vagi or the sympathetic system does not prevent the passage of the chyme from the stomach into the intestines. There is no question, however, that the sphincters of the stomach are partially controlled by the central nervous system. With special reference to the cardia, Langley<sup>2</sup> has shown that the vagus contains both inhibitory and accelerator fibres, while Openchowski<sup>3</sup> has demonstrated that stimulation of the sympathetic increases the contraction of the cardia. In reference to the pylorus, May<sup>4</sup> has shown that the stimulation of the vagus causes at first an inhibition followed by an acceleration of the contraction of the pylorus. In regard to the nervous mechanism of other portions of the stomach, May has demonstrated that stimulation of the vagus caused at first an inhibition of the peristalsis of the pyloric portion,

<sup>1</sup> *Am. Jour. Physiol.*, 1905, xiii, p. 22.

<sup>3</sup> *Centralblatt für Physiologie*, 1889, S. 1.

<sup>2</sup> *Jour. Physiol.*, 1898, xxiii, p. 407.

<sup>4</sup> *Jour. Physiol.*, 1904, xxx.

with a lessened tone of the cardia, followed later by an acceleration of peristalsis in the pyloric region with increased tone in the cardia. Cannon<sup>1</sup> has shown that emotion plays an important rôle in the movements of the stomach by demonstrating that peristalsis ceases whenever "the animal manifests signs of rage, distress, or even anxiety." According to Cannon<sup>2</sup> the stomach is divided into two parts that are physiologically distinct. The larger part is the cardiac area, the smaller the pyloric. During the process of digestion there are constant peristaltic movements running over the surface of the pylorus. Peristaltic waves are not present in the cardiac area. After the pylorus empties itself, however, the cardiac portion produces a tonic pressure, forcing its contents into the pyloric area; therefore, mixture with the gastric secretion takes place in the pyloric area. The food remains, however, for some time in the cardiac area, during which the salivary digestion is continued. According to Cannon the presence of free hydrochloric acid in the stomach occasions the relaxation of the pyloric sphincter, causing the pylorus to open and so permit the escape of the acid chyme into the duodenum. The presence of the acid in the duodenum produces a reflex stimulation of the pylorus, which closes and remains so until the contents of the duodenum have again become alkaline.

Cannon, who has pointed out the importance of tonus in the activity of the alimentary canal, has shown that mechanical stretching stimulates activity in smooth muscles, and as this form of muscle surrounds the stomach, and intestines (which fill up and then empty), the effect of the distension becomes manifest. Thus when the muscle is in a state of tonus, stretching is followed by a contraction, but when the stomach is atonic, flaccid distension is not followed by contraction. According to Cannon "the view that tonicity of the neuromusculature of the alimentary canal is a fundamental necessity for the appearance of rythmical movements harmonizes many diverse observations." It accounts for the lack of motility in atony of the stomach, and gives an explanation for the existence and importance of extrinsic motor nerves. It also explains why worry, anxiety and distress inhibit gastro-intestinal movements, for such conditions accompanied by splanchnic impulses abolish tonus.

**Etiology.**—Gastric neuroses may be primary or secondary; they are primary when the seat of the nervous disorder is inherent in the stomach itself, and secondary when the nervous mechanism of the stomach is reflexly affected either from the brain, spinal cord, or some other organ, such as the liver, kidneys, etc. Thus, a severe pain, such as kidney colic, may reflexly affect the stomach, causing vomiting; it is also a well-known fact that menstrual disorders, as well as sexual disorders in males, may have a marked reflex effect upon the gastric functions. It has been shown by Gould that severe eye-strain may also have a marked influence in this regard. On the other hand, gastric neuroses may in turn reflexly affect other organs, and we may find such symptoms as headache, palpitation, insomnia, and other manifestations.

<sup>1</sup> *Am. Jour. Physiol.*, 1898.

<sup>2</sup> *Ibid.*, 1904.



**Occurrence.**—The writer has classified the cases of gastric neuroses occurring in his practice during a period of some years; in order to obtain a clearer view of these cases, the histories have been collected both from the records of private cases and hospital practice. This plan was deemed advisable because comparatively few forms of gastric neuroses are seen in the hospital wards. Of 2000 patients suffering with the various forms of gastric disease, 1592 (79.6 per cent.) represented one or more forms of nervous disorder, while 408 (20.4 per cent.) were affected with organic disease. In a smaller series of cases more recently analyzed, it has been observed that gastric neuroses are much less frequent now, than was formerly supposed, and that but 55 per cent. of the cases could be classified as neuroses, while 45 per cent. represented organic diseases. This change in the relation of two conditions, is due to the fact that many cases which were formerly classified as neuroses are known now to be due to some definite pathological change.

In order that a gastric neurosis may exist, there must be present some predisposition, *i. e.*, a neurotic condition in the individual. This is frequently first manifested by nervous symptoms directed to other organs, the stomach only later becoming involved. In this series of cases the early nervous manifestations were first noted in 38 per cent. in organs other than the stomach, while in 62 per cent. the stomach itself was first involved. The manner of development of these affections is often peculiar, at times beginning suddenly, often without any apparent cause or error in diet, persisting for a longer or shorter period of time, and then perhaps terminating abruptly, at other times coming on slowly, progressing rapidly, and terminating when least expected. Heredity plays an important rôle in the development of gastric neuroses. Among our observations 70 per cent. of the patients gave a history of either some functional or some organic hereditary nervous tendency. In 32 per cent. the disorder was directly dependent upon some shock, anxiety, or vice, while in 18 per cent. no known cause could be discovered.

Most of these affections are more frequently observed in females than in males, more often in men of the higher classes, and about equally in females of the lower and higher classes. In this series of cases 54 per cent. represents the number of females affected, while 46 per cent. indicates the number of males. The chief factor in the production of these conditions in males is overwork, worry, and excesses, especially overindulgence in drink, 29 per cent. of the patients giving a distinct alcoholic history. The chief causes in women are disorders of menstruation and reproduction, anxiety, sorrow, and disappointments. The predominance in this sex is due to the mode of living and peculiar affections.

**Age.**—The neuroses rarely begin in old age. They occur most frequently between the twentieth and fortieth year. The following table shows the age in the gastric neuroses in this series:

Year.	Cases.	Per cent.
1 to 20 . . . . .	232	14.5
20 to 30 . . . . .	354	22.5
30 to 40 . . . . .	404	25.0
40 to 50 . . . . .	339	21.5
50 to 70 . . . . .	175	11.0
60 to 70 . . . . .	88	5.5



The neuroses occur as frequently in the robust and well-nourished as in the broken-down and enfeebled individual. After persisting for some time neuroses interfere with the general health, frequently occasioning emaciation; this condition, however, is secondary in most instances and is not a predisposing factor in the etiology. The symptoms of a general neurosis are usually present, *i. e.*, irritability, lassitude, insomnia, depression, and a feeling of malaise. Hyperesthesia or anesthesia often exists in certain parts of the body. The subjective symptoms are changeable and capricious, exhibiting protean changes in rapid succession. The digestion is usually, as Boas states, in a condition of "labile gastrointestinal function." The digestive complaint is frequently independent of the quality and quantity of food ingested, and without any connection with its digestion; errors of diet are not necessarily followed by aggravation of the symptoms. Periodic attacks of discomfort often alternate with unaccountable periods of well-being. Frequently sudden changes take place in the secretory or motor functions of the stomach, or in both, so that a superacidity may quickly give way to a subacidity and a motor insufficiency to a hypermotility. The pain which may be present is diffuse and often bears no relation to the digestion of food.

Gastric neuroses are usually polysymptomatic, more rarely monosymptomatic in character. In the first form there is a multiplicity of symptoms, while in the latter but one symptom is observed. Neuroses rarely present the same form during their entire period, and a monosymptomatic neurosis is not infrequently converted into the polysymptomatic form. A characteristic feature of gastric neuroses is the fact that the symptoms vary so frequently, which is often of great assistance in differentiating between this class and organic disease.

**Classification of Gastric Neuroses.**—The classification into secretory, sensory, and motor neuroses, so often used, has by no means been found to be satisfactory, and Boas<sup>1</sup> has suggested the following modification:

#### MONOSYMPTOMATIC GASTRIC NEUROSES

##### *Irritative Group.*

Superacidity or hyperchlorhydria.  
 Supersecretion or gastrosuccorrhœa.  
 Gastromyxorrhœa.  
 Bulimia.  
 Parorexia.  
 Gastralgokenosis.  
 Gastralgia.  
 Hyperesthesia.  
 Rumination (mercism).  
 Regurgitation.  
 Eructatio nervosa.  
 Vomitus nervosus.  
 Nausea nervosa.  
 Cardiospasm.  
 Pylorospasm.  
 Pneumatosis.  
 Peristaltic unrest.

##### *Depressive Group.*

Subacidity or hypochlorhydria.  
 Anacidity or achylia gastrica.  
 Akoria.  
 Anorexia.  
 Sitophobia.  
 Incontinence of pylorus.  
 Atony.

#### POLYSYMPTOMATIC GASTRIC NEUROSES

Nervous dyspepsia.

<sup>1</sup> *Deut. med. Wochenschrift*, August 17, 1906.

**Diagnosis.**—This may be very difficult, as frequently these conditions envelop some organic disease, the nervous symptoms being so much more prominent that the actual disease becomes entirely masked. In order to establish the nervous character of a gastric disorder, all organic diseases must be excluded, and this is frequently a most difficult task. In the monosymptomatic forms the diagnosis is usually simple, especially if the examination of the gastric contents and functions shows a normal condition. The patient frequently has a hereditary nervous tendency or a weakened nervous system or neurotic habit. The disease is frequently either characterized by peculiar periodical or paroxysmal attacks, with many unaccountable periods of well-being, or by an absence of subjective symptoms even upon the ingestion of indigestible food.

The diagnosis of the polysymptomatic forms is more difficult. In these the symptoms that are frequently found in severe organic diseases may be interwoven and combined with the gastric neuroses; a further difficulty arises from the fact that organic disorders are often accompanied by nervous symptoms, and a most careful investigation may be necessary. Nervous dyspepsia is the most typical example of the polysymptomatic neuroses with a multiplicity of symptoms seldom found in its frequency in organic diseases of the stomach. The nervous dyspeptic himself often indicates the diagnosis of this condition, and one need only listen to his story attentively. Objective signs may be absent, or, when present, may mislead one; thus a slight dislocation of the kidney or a slight gastric atony would be insufficient to account for the symptoms present. In the diagnosis of these conditions the appearance of the attacks without apparent cause and the intervals of well-being are most striking. The fact that as a rule the complaints of the patient bear no relationship to the quantity and quality of food ingested, but are mainly dependent upon overexertion, mental disturbances, and excitement is of greater value in the diagnosis. The conditions are often relieved or improved by change of scene or relaxation.

When it is impossible to gain a clear idea of the condition, Boas advises the functional testing of the stomach. The patient is given a very digestible diet, such as is usually prescribed during the third week of an ulcer treatment. The subjective symptoms are noted while the patient is on the diet, during a period of from three to four days; then additions are made gradually, such as sauces, vegetables, dessert, and raw fruits. An exact record is again made, and by comparing the symptoms during the first and second period the presence of an organic or nervous gastric disorder will be indicated. In the latter condition the symptoms not only often diminish, but frequently disappear entirely during the second period, while in the former they are apt to increase. Boas also advises the frequent testing of the motor and secretory functions of the stomach, which when found to be constantly normal are often alone sufficient evidence to indicate the neurotic nature of the disorder.

**Prognosis.**—The prognosis in neuroses of the stomach is very favorable, provided the condition is treated early and the cause discovered and removed. Relapses, however, are frequent if care is not taken to regulate the daily regimen and maintain, so far as possible, a stable condition of

the general nervous system. It is not uncommon, when relapses do occur, that some nervous manifestation is produced other than that which was originally present. In the series of 1592 cases there were 752 (47 per cent.) that gave a history of one or more relapses; of these, 321 (20 per cent.) had one and 431 (27 per cent.) more than one relapse; in the remaining 840 no evidence of any former attacks could be obtained.

**Treatment.**—In this it is necessary to remember that one is dealing with patients whose imagination is easily influenced in directions other than normal; for this reason the personal influence of the physician himself will have much to do with the patient's recovery. It is at first always important to make a most careful and complete examination to convince the patient that there is no organic disease. A change of scene is often important, and specific rules as to the mode of living and diet should be insisted on. In some cases a sanatorium treatment is most desirable. The diet should be carefully regulated, and especially in badly nourished patients the aim should be to strengthen the individual and add to his nutrition by increasing the body weight. For this purpose also the physical methods of treatment are most serviceable and must be resorted to, acting at the same time as suggestive measures. Of these, massage, cold and warm douches, packs, poultices, intragastric as well as external electricity, douching and lavage of the stomach play a most important rôle.

Sadger<sup>1</sup> extols hydropathic treatment for these conditions, and adapts the treatment to the constitutional weakness of the patient rather than to special symptoms. The treatment in this direction must be tonic and stimulant. He advises cold sponging with rubbing, cold compresses, the half or full cold bath, the Scottish douche, and Winternitz's compress. When sanatorium treatment is impossible or impracticable, a sojourn at the seashore or mountains, with specific directions as to the mode of living, rest, exercise, and diet, often proves serviceable. A cure at some mineral spring is often beneficial, provided the proper spring is selected and specific directions given as to drinking the water and the mode of living to be followed. In no instances should patients suffering with nervous stomach troubles be permitted to tell others of their condition. In severe forms a rest cure should be resorted to, as most remarkable results can often be achieved by this means.

The nervous dyspeptic should be taught to rely more upon proper hygienic measures than upon drugs, as but few drugs have any marked influence in these cases. Of these remedies the bromides, preparations of valerian, arsenic, and codeine are most useful.

### HYPERACIDITY OR HYPERCHLORHYDRIA

By the term hyperacidity is meant an excessive flow of gastric juice or, more correctly, an increase in the secretion of the hydrochloric acid produced by the gastric mucous membrane during the process of digestion.

<sup>1</sup> *Archiv f. Verdauungskr.*, Bd. xii, Heft i.



It has been questioned whether hyperchlorhydria should be termed a distinct disease, inasmuch as the excess of acid is simply a symptom observed in a number of gastric disorders and due to a variety of causes; yet the symptoms associated with this condition are so definite and so often embrace all subjective manifestations that we are forced to treat this condition as a special clinical entity. Yet it must be noted that although hyperchlorhydria is in many instances a secretory neurosis, in a large number of cases it is associated with some definite lesion.

The question as to what is meant by an excess of hydrochloric acid has not yet been thoroughly agreed upon by all writers. According to Ewald, Einhorn, and others the normal percentage of free hydrochloric acid one hour after the Ewald test breakfast ranges between 0.1 and 0.2 per cent. Any amount above 0.2 per cent. is to be considered a hyperacidity; on the other hand, many cases are met with having a greater acidity than 0.2 per cent. without symptoms of hyperacidity. In 14 of the patients in this series with free hydrochloric acid ranging between 0.21 and 0.29 per cent., and a total acidity varying from 70 to 100, there were no evidences of any gastric disturbance whatever.

On the other hand, symptoms of hyperacidity may exist even in cases of hypochlorhydria. This has occurred in 11 of the series. In the largest proportion of cases, however, any increase above 0.2 per cent. free hydrochloric acid represents a superacidity, and is usually accompanied by symptoms of this condition, although this is not always the case, for there are patients with acidities as high as 0.29 per cent. without any symptoms whatever, and others in whom free hydrochloric acid is entirely absent in whom symptoms of hyperacidity are manifested. The very same amount may indicate a hyperacidity in one individual and not in another, showing that individual variations may exist in the normal percentage, and that we cannot always draw a sharp line between the normal and the hyperacid state. The condition has been explained in two ways; according to some writers, the stomach of each individual has its own degree of acidity, and thus may perform its function with an acidity which is insufficient or more than sufficient for another. Therefore, any increase in this normal proportion of acid will render this particular gastric secretion superacid for this individual and occasion symptoms of hyperchlorhydria. Another explanation which seems to be more satisfactory was suggested by Talma.<sup>1</sup> According to this observer the symptoms of hyperchlorhydria are due in these cases to a hypersensitiveness or hyperesthesia of the gastric mucosa to hydrochloric acid. Stockton pointed out that the gastric mucosa is not only often intolerant to an excess of hydrochloric acid, but often to a normal or subnormal percentage of acid. Steele confirmed the observation, and went a step farther to show that the hyperacid condition of the gastric contents is not alone capable of producing the symptoms in hydrochlorhydria; according to him there must be some other condition present occasioning the gastric hyperesthesia, producing that condition in which the gastric mucosa cannot tolerate a normal or abnormal amount

<sup>1</sup> *Zeitschrift f. klin. Med.*, 1884, Bd. xiii.



of acid, and, further, this hyperesthesia is due to ulcer, retention or hypersecretion on the one hand, or to a sensory neurosis on the other. Kaufmann also believes that some other factor must be involved to occasion the symptoms of hyperacidity besides merely the increased amount of the secretion. According to him, whenever the patient presents the symptoms of hyperacidity a second pathological factor must be sought, forming the connecting causal link between the chemical findings and the subjective disturbances. In many of these cases this factor is demonstrated in some ulceration, erosion, dilatation, and by far most frequently in an atony of the stomach.

**Etiology.**—Hyperchlorhydria is the most frequent of all gastric disturbances. In the series of 2000 cases, representing organic as well as functional disturbances of the stomach, there are 1273 (63 per cent.) showing a hyperacidity; in the series of 1592 cases of gastric neuroses there are 542 cases of hyperchlorhydria, or 34 per cent.

The disease is frequently observed in young and middle-aged persons, while it is rarer in older individuals. It is found to a slight degree more frequently in females than males. Hyperchlorhydria is found more frequently among the better and wealthier classes than among the poor. This is due to the fact that mental strain and worry are often direct factors in the production of this disorder. Jaworski points out its frequency among the Polish Jews; we have observed it as a most frequent condition among the Hebrews of this vicinity. The following etiological factors in its production may be noted:

1. Mental strain, mental overwork, prolonged worry, and mental fatigue are important. Nervous individuals and persons who have undergone severe mental strain are especially prone to this disorder; Van Noorden has found it frequently in patients suffering with melancholia. Neurasthenia and hysteria are also important causative factors; of the 542 cases of hyperchlorhydria, 186 belong to this class.

2. Gastro-intestinal atony is a marked etiological factor, especially those forms associated with chronic constipation. It occurred in 164 of this series, mainly in young females.

3. Indiscretions in diet, such as the use of food of a very heavy character, as well as the abuse of alcoholic drinks and tobacco, are the cause of the largest proportion of cases of hyperchlorhydria. This condition is frequently found in persons who masticate their food imperfectly, who eat too quickly, who drink foods too hot or too cold, or take their foods too highly seasoned. This class is represented by 186 cases.

4. Among other conditions that bear some etiological relationship are ulcer of the stomach, chlorosis, cholelithiasis, nephrolithiasis and appendicitis but it is not our province to discuss the connection between ulcer and hyperchlorhydria here. Oswald pointed out the association of hyperacidity with chlorosis; in 85 per cent. of his cases a hyperchlorhydria existed. In 34 cases of this series with chlorosis and gastric disturbances, hyperacidity was found in 24, normal acidity in 8, and subacidity in 2 cases. Cholelithiasis is frequently accompanied by hyperacidity and any condition leading to biliary retention may produce this condition.

The following table represents the cases of hyperchlorhydria, tabulated according to age and sex, presenting the various etiological factors:

Causes.	No.	Males.	Females	Ages in years.		
				10-30.	30-50.	50-70.
1. Mental overwork and fatigue, neurasthenia . . . .	156	89	67	44	71	41
2. Gastro-intestinal atony with chronic constipation . . . .	164	54	110	73	54	37
3. Indiscretions in diet, food, drink, and tobacco . . . .	186	105	81	95	57	34
4. Indefinite and unknown causes	36	15	21			

**Pathology.**—As hyperchlorhydria is largely a sensory neurosis, no anatomical lesion is present in the greater proportion of cases. Oesterreich<sup>1</sup> found the gastric mucous membrane perfectly normal with the exception of a few slight erosions in a patient suffering from hyperchlorhydria dying of an intercurrent pneumonia. According to Hemmeter,<sup>2</sup> who has examined fragments of mucosa found accidentally in the wash water, there is in more than one-half the cases of hyperacidity “a proliferation of the glandular elements and increase of oxyntic or border cells.” Straus<sup>3</sup> described similar lesions.

**Symptoms.**—The subjective symptoms usually appear gradually; they consist of acid eructations, heartburn, and pain and burning in the stomach. Acid eructations usually appear at the height of the paroxysms of gastralgia, and their appearance is accompanied by a passing relief from pain. If portions of the acid secretion of the stomach are eructated, the mucous membrane of the œsophagus is subjected to this irritation, and heartburn develops. This symptom usually appears after eating acid foods, and is frequently relieved by taking milk, meats, and eggs. The pain may vary from a severe pressure in the stomach to a very acute pain, and may extend into the back between the shoulder-blades and pass under the sternum to the pharynx (pyrosis hydrochlorica). It is not continuous, but appears at certain periods with intervals of complete relief, usually from two to four hours after meals, depending upon the quality and quantity of food taken. In a very small number of cases the pain supervenes immediately upon eating, as occurred in 9 of the series (1.6 per cent.). The symptoms continue for a variable period of time, disappearing in the course of an hour or persisting for many hours. Pain is much more easily induced by starchy foods than by protein foods, more quickly by light meals than by heavy ones, and is usually relieved by the ingestion of food or by neutralizing the acid by means of some alkali. Paroxysms of pain (gastralgia) occur in a certain proportion of cases; they develop gradually, beginning as a feeling of pressure and becoming more severe. As a rule, the pain disappears at night upon lying down, and does not begin again until several hours after breakfast.

The severe gastralgic paroxysms are not commonly found after every meal. They are accompanied not only by intense pains in the epigastrium, but also in the back; they are partially relieved by the acid

<sup>1</sup> *Deut. med. Wochenschrift*, 1895, Nr. 21.

<sup>2</sup> *Archiv f. Verdauungsk.*, Bd. iv, S. 23; *Diseases of the Stomach*, third edition, p. 814.

<sup>3</sup> *Virchows Archiv*, 1898, Bd. cliv.

eructations and entirely by the vomiting of the acid secretion, which burns the throat and numbs the teeth as it passes over them. In some cases the seizures may be very mild, and in other cases they recur irregularly at intervals of days. In this series of 542 cases, gastralgic seizures occurred in 176, *i. e.*, 32 per cent. A sensation of burning in the stomach is frequently observed; this is felt in the epigastrium, and may extend to the back. It is relieved by the same measures as those which relieve the pain, namely, by alkalis or the taking of some form of food. In this series there were 221 that complained of this sensation, *i. e.*, 40 per cent. The appetite is usually good, and as eating usually relieves the symptoms, the patient often accustoms himself to eat frequently; small quantities will, however, often satisfy the patient. In 124 (21 per cent.) of the cases the appetite was increased, in 357 (66 per cent.) it was normal, and in 61 (13 per cent.) it was diminished. The thirst is not greatly increased, although the reverse is stated by most authorities. In this series thirst was only increased in 31, *i. e.*, 6 per cent.

The bowels are frequently constipated, as occurred in 164 of the series, or 30 per cent. Occasionally constipation alternates with diarrhoea, as occurred in 7 of the cases (1.3 per cent.).

The objective symptoms may be divided into two classes, those presented by the physical examination and those obtained by the examination of the vomited material and gastric contents. The patient, as a rule, is in good general health, has lost but little flesh, and the general nutrition is not usually disturbed; the abdomen is not usually sensitive to pressure, and painful areas are not apparent except perhaps during the attacks of pain, when the stomach may be found distended and sensitive to pressure. Vomiting is not frequent; it usually occurs when the paroxysms of gastralgia are present, and then at the height of the attack; relief is obtained by vomiting, and the pain disappears. This symptom occurred in 86 of the cases, or 15 per cent. The vomited matter is very acid, which is detected even by the patient himself; on examination this material is found to contain large quantities of free hydrochloric acid. The examination of the gastric contents after a test meal usually reveals normal or hypermotility. Six hours after a Riegel test dinner the stomach is usually empty; one hour after a test breakfast it contains only a small quantity of gastric juice. In 30 per cent. of this series there was an atony of the stomach in which more or less retention was observed. The gastric juice shows a very high degree of acidity; the starch digestion is imperfect, and rather large quantities of amidulin are found. On the other hand, the protein digestion in the stomach is complete and peptonization is more rapid than under normal conditions, so that none or but few undigested meat fibres are found in the gastric contents.

Schüler<sup>1</sup> has pointed out that the specific gravity of the gastric juice is diminished in hyperchlorhydria. According to this observer it is usually below 1.016, the normal specific gravity varying between 1.016 to 1.020. The observations in 14 cases as to the specific gravity of the

<sup>1</sup> *Deut. med. Wochenschrift*, May 10, 1900.



gastric contents in this condition are, on the whole, in accord with those of Schüller, ranging between 1.008 and 1.014, although occasionally higher figures are found, as in 3 of this series between 1.019 and 1.022.

Absorption in the stomach is said to be more rapid in hyperchlorhydria than under normal conditions.

The urine is at times alkaline and contains a precipitate of phosphate, especially after severe attacks of vomiting. The acidity of the urine is diminished proportionately to the increase in acidity of the gastric juice, and the chlorides are also diminished in quantity.

**Diagnosis.**—This is established by careful investigation into the subjective symptoms together with the results obtained from analysis of the gastric contents. These symptoms consist of acid eructations, heartburn, burning and pains in the stomach, the pain appearing from two to four hours after meals, relief being obtained by the ingestion of food and by neutralizing the acid with alkalis. The examination of the stomach contents after a test meal reveals an increase in free hydrochloric acid; while on fasting, the stomach is found nearly or almost completely empty. Hyperchlorhydria must be differentiated from chronic hypersecretion, ulcer, acid gastritis, atony, and cholelithiasis.

*Chronic hypersecretion* is distinguished by the intense gastric pains appearing frequently at night, the more frequent vomiting, and the appearance of large quantities of gastric juice (100 cc. and more) in the fasting stomach. *Ulcer* of the stomach (without hemorrhage) is differentiated by the presence of the circumscribed epigastric and dorsal areas of pain. The pain in ulcer is proportionate to the quality and quantity of the food taken, which is not usual in hyperchlorhydria. Occult blood is frequently found in the feces in ulcer, but not in hyperchlorhydria. *Duodenal ulcer* is distinguished by the characteristic remissions in pain, extending over longer or shorter periods; by the painful area which is absent in hyperacidity, and by the presence of occult blood in the stools. The differential diagnosis between these two conditions is very difficult at times, as hyperacidity usually accompanies ulcer of the stomach and duodenum; the greater irregularity of the symptoms in hyperchlorhydria and presence at least of some of the definite symptoms of ulcer will usually lead to a correct diagnosis. In doubtful cases, Boas advises that the patient undergo the rest treatment for ulcer; a favorable outcome rather indicates the presence of ulcer.

Hyperchlorhydria is distinguished from an *acid gastritis* by the constant absence of mucus in the gastric contents, and from *atony* by the absence of symptoms of retention. In a certain proportion of cases of hyperchlorhydria, however, atony is present (30 per cent.) and the symptoms of both conditions become marked. In *cholelithiasis* the pains are not relieved by the ingestion of food or the administration of alkalis, and radiate to the right toward the hypochondriac region and are in no way dependent upon the time of the ingestion of food, whereas the pains of hyperchlorhydria usually appear at the height of digestion, *i. e.*, from two to four hours after meals.

**Prognosis.**—This is usually quite favorable as to the relief of the symptoms, especially if the condition is of recent origin; in protracted



cases the prognosis is less favorable, and even when patients have been apparently cured of this condition relapses are not infrequent, probably due in many instances to the fact that while at first the acidity of the gastric secretion may be reduced, a permanent reduction is not usually effected. In personal observations in 9 patients in whom we have been able to make gastric analyses more or less frequently during the time of treatment, *i. e.*, for a period of six months, and again after the first and second years, during which symptoms of hyperacidity no longer existed and treatment was no longer instituted, it is evident that while the patient is under treatment and the acidity of the gastric juice can be reduced, this reduction is not permanent, and that while the patient may be free of all symptoms of hyperacidity an excess of acid secretion still exists. This points to the fact that our treatment is only effectual in reducing the gastric hyperesthesia and not the acidity.

In those instances in which the hyperacidity is symptomatic of other conditions the prognosis depends upon the relief of the primary disease. In the series of 542 cases of hyperchlorhydria in which it was possible to follow 48 cases for a period of at least three years or more, 31 were cured (65 per cent.), 10 were relieved (21 per cent.), and 7 were not benefited (14 per cent.); relapses occurred in 5 cases (10 per cent.).

**Treatment.**—In this the diet plays the most important rôle, it being essential that the food should be given in such a form as not to produce any irritation to the mucous membrane of the stomach. As the gastric hyperesthesia is mainly responsible for the hyperacidity, the treatment should be directed to this condition. This would include the removal of all causes of irritation, the prohibition of alcoholic stimulants; all acids, including organic acids, should be forbidden; all spices and condiments, such as ginger, pepper, mustard, and horse-radish, should be prohibited. All foods to which vinegar or lemon-juice have been added should be interdicted; all hard substances which are apt to irritate the stomach, such as nuts, should be avoided; food must be thoroughly masticated and should be taken neither too hot nor too cold. Formerly a diet consisting almost exclusively of proteins was recommended in order to neutralize as much acid as possible as the proteins possess the power of combining with free hydrochloric acid. On the other hand, it was soon discovered that while the proteins possess this power, they nevertheless again stimulate the flow of acid; some, such as raw beef, beef-juice, and beef extract, more than others, such as well-cooked meat.

More recently various authors have recommended a carbohydrate diet in preference to a protein one. Some prefer a liberal mixed diet, consisting of proteins, fats, and carbohydrates. The following table taken from Bickel presents the food which slightly and the food which strongly excites gastric secretion:

*Foods slightly exciting acid secretion.*

Liquids: Water, alkaline water, tea, cocoa (rich in fats), milk (rich in fats), cream, and egg-albumen.

Condiments: 0.9 per cent. of salt solution.

Solids: Cooked meats, fats of all kinds, cooked vegetables, such as potatoes, asparagus, cauliflower, spinach, white beets (all in purée), starch, sugar.

*Foods strongly exciting acid secretion.*

Liquids: All alcoholic and carbonated drinks, coffee, cocoa (poor in fats), skimmed milk, beef-tea, beef extract, strongly seasoned soups, yolk of eggs, hard-boiled eggs, beef solution.

Condiments: Pepper, cinnamon, mustard, cloves, paprika, salt in concentration.

Solids: Raw or slightly cooked beef, dark meats, salted meats (pork, pickled meats, smoked fish), dark breads.

The carbohydrate foods which are allowable are the more digestible vegetables, such as mashed potatoes, spinach, asparagus, peas, and carrots, strained and eaten in the form of purées, also the digestible farinaceous foods, such as rice and grits. Strauss<sup>1</sup> has recommended the administration of a solution of sugar; this food can be best given in most instances in the form of some baked cake in which part of the starch has become dextrinized by baking or roasting. Strauss and Aldor have advised the use of fats, inasmuch as they tend to lessen the acidity of the gastric secretion. They are best given in the form of butter, cream, olive oil, and the like. Of the fluids, milk, cocoa, and alkaline mineral waters, such as Apollinaris, Vichy, and Seltzer, are especially useful; the carbon dioxide produces a sedative effect and lessens the secretion of acid. These waters may be used to dilute milk.

In arranging the diet it has been found best in dealing with patients taking but little nourishment to allow them to eat at frequent intervals; if, however, large meals are consumed, it is advisable to permit only three meals a day, allowing the stomach to rest in the intervals. In marked forms of nervous hyperchlorhydria a purely vegetable or milk and vegetable diet has been recommended by certain writers; the vegetables should be eaten in the form of purées. Laufer, Vincent, Euriquez, and others attach great importance to a salt-free diet in hyperchlorhydria, believing that a high percentage of muriatic acid may be reduced by a diet free of salt. Zweig comes to similar conclusions, and urges a salt-free diet in the treatment of gastric hyperacidity. In advanced cases, with marked emaciation and prominent nervous symptoms, an absolute or modified rest cure will accomplish excellent results; in these cases milk and egg-albumen should be the only food given at first, gradually increasing, and finally allowing easily digestible solid food.

The following list, taken from Friedenwald and Ruhrah,<sup>2</sup> gives the foods which are allowable and those which are forbidden in hyperchlorhydria: Allowable: Eggs, soft boiled, hard boiled, or poached. Meats, boiled or broiled; brains, raw scraped beef, boiled or broiled beef, broiled steak, roast mutton, broiled chops, roast lamb; boiled, broiled, or roasted chicken; broiled or roasted squab, roast turkey, broiled or roasted birds. Farinaceous food: Rice, cornstarch, sago, tapioca, arrowroot, hominy, grits, vermicelli, cream of wheat, stale wheat bread, toast corn bread, pulled bread, zwieback. Fruits: Baked or stewed apples, stewed apricots, stewed peaches, stewed pears, stewed prunes. Fatty foods: Butter, cream, pure olive oil. Drinks (taken mainly between meals): Milk, buttermilk, malted milk, peptonized milk, milk with lime-water, milk with Vichy, milk flavored with tea, milk flavored with coffee, kefir,

<sup>1</sup> *Zeitschrift f. klin. Med.*, vol. xxix.

<sup>2</sup> *Diet in Health and Disease*, fourth edition, p. 810.

koumyss, junket, whey, cocoa, albumin-water, water (not with meals), hot water. Vichy, Apollinaris, Poland, Lithia water, Carlsbad.

They must not take: Soups, fried foods, pork, veal, stews, hashes, corned meat, liver, kidney, duck, goose, sausage, crabs, lobsters, preserved fish, smoked fish, salmon, salt mackerel, sardines, cauliflower, celery, cocoa, radishes, cucumbers, sweet potatoes, beets, tomatoes, acid fruits, salads, hot bread or cakes, nuts, candies, pies, pastry, strong tea, coffee, alcoholic stimulants, ice-water, ice-cream.

**Hygienic Measures.**—These should never be neglected in the treatment of hyperchlorhydria. Those patients who have been fatigued by overwork should be ordered rest, and those who are worn out by mental strain and excitement are often best ordered away to the country, seashore, or mountains; physical exercises, out-door life, and cold sponge baths are often serviceable adjuvants; warm poultices or Preissnitz compresses are frequently useful in the relief of pain.

Gastric lavage is rarely necessary in the simple cases although it is often of benefit in severe and obstinate forms. It is best practised late in the evening, three or four hours after the last meal, or on an empty stomach in the morning; douching of the stomach with a solution of silver nitrate is often beneficial; 500 cc. of a 1 to 2000 solution is allowed to enter the stomach and again washed out thoroughly with normal salt solution. Electricity often exerts a very beneficial effect in some cases of hyperchlorhydria, and can be used either as the intragastric faradization or galvanization. The faradic current is useful in most instances, but in painful conditions the galvanic current is to be preferred. The chronic constipation often associated with hyperchlorhydria is frequently relieved by this mode of treatment.

**Medicinal Treatment.**—Alkalis are employed to neutralize the excess of acid. Of these, the bicarbonate of soda, calcined magnesia, magnesia carbonate, calcium carbonate, and the phosphate of soda are most frequently utilized. Calcined magnesia has an advantage over bicarbonate of soda, as the former neutralizes four times as much acid as the latter; it has the additional advantage in that it is distinctly laxative and is therefore especially useful when constipation is present; the doses of the alkali should be, so far as possible, proportioned to the heaviness of the meal as well as the degree of hyperacidity. The alkalis should be administered when the discomfort begins to manifest itself, *i. e.*, about two hours after meals. Of other drugs found useful are:

1. Atropine, which inhibits gastric secretion. This remedy can be administered in the form of the extract of belladonna or atropine.

2. Nitrate of silver in solution, which tends to diminish the gastric hyperesthesia.

3. Bismuth subnitrate and carbonate, which may be administered in large doses and which exert a beneficial, largely mechanical, effect on the gastric mucosa.

4. Hydrogen peroxide is also useful and may be given in one-teaspoonful doses in a glass of water after meals. Magnesium peroxide, known under the trade name as magnesium perhydrol, has also been found beneficial.



5. The nerve sedatives, such as the bromides, valerianates, and sumbul, which relieve the gastric hyperesthesia. In those cases in which symptoms of hyperacidity exist and in which the gastric secretion shows a normal or lessened amount of acid the sedatives are more valuable than the alkalis.

6. *Nux vomica*: While the bitter tonics are to be avoided, as a rule, in hyperchlorhydria, Musser<sup>1</sup> advised the administration of *nux vomica* in ascending doses in those cases in which the symptoms of hyperacidity are due to a sensory neurosis; he had uniformly good results from this.

7. Olive oil: Cohnheim<sup>2</sup> has recommended olive oil very highly in the treatment of this condition. It may be given in tablespoonful doses before meals or about two hours after meals.

Inasmuch as constipation is sometimes the cause of hyperchlorhydria, a correction of this will often give permanent relief and this is often best accomplished by diet rather than by drugs.

Of the watering places for the treatment of hyperchlorhydria, Carlsbad, Vichy, Neuenahr, and Bedford and Saratoga (Vichy) are to be most highly recommended.

**Larval Hyperacidity.**—Straus<sup>3</sup> was the first to point out that symptoms of hyperacidity may exist without an actual increase in hydrochloric acid, and Roth and Straus<sup>4</sup> explain this by assuming that there is an actual hyperacidity which is not revealed, because the examination of the gastric contents is made an hour after the test breakfast is given, and that two elements exist in the formation of the gastric secretion—an inactive diluting fluid and an active form whose specific action is to digest proteins. The active digestive secretion is gradually diluted by the diluting fluid. It is, therefore, easily conceived how, if the diluting fluid be secreted rapidly, a gastric juice which is hyperacid when first secreted may be rapidly reduced to normal or subnormal.

According to our observations<sup>5</sup> the symptoms are largely those of a neurasthenia, evincing at the same time special manifestations of hyperchlorhydria, consisting of pain and pressure in the region of the stomach one hour after meals, and extending over a period of from one to one and one-half hours, and usually relieved at the end of this time, or at any time, by the ingestion of food. Of the other symptoms, acid eructations, heartburn, nausea, and occasionally vomiting of acid material are most prominent. The appetite is usually increased, though on account of the pain induced by the ingestion of food there is usually fear of eating. An epigastric painful area is not present and occult blood is always absent in both gastric contents and in the stools. In all instances general nervous symptoms are manifested, as headaches, insomnia, lassitude, irritability, and depression, with periods of discomfort alternating with accountable periods of well-being, the periods of discomfort often being induced by nervous influences. The quantity of gastric contents obtained

<sup>1</sup> *Transactions of the Association of American Physicians*, 1905, p. 193.

<sup>2</sup> *Zeitschrift f. klin. Med.*, vol. iii, S. 110.

<sup>3</sup> *Deut. Archiv f. klin. Med.*, 1896, Band lvi, S. 120.

<sup>4</sup> *Zeitschr. f. klin. Med.*, Band xlvii.

<sup>5</sup> *Am. Jour. Med. Sci.*, 1911, cxlii, p. 157.



is always large, varying between 215 and 368 cc., always a most significant feature of this condition. The appearance of the contents is also characteristic, consisting largely of a watery secretion containing but little sediment. On standing, two layers are formed—a lower, slight in amount, but with solid sediment, and above a clear layer, larger in quantity. The total acidity as well as the percentage of free hydrochloric acid is always normal, though in the earlier period of digestion a high total acidity as well as a marked hyperchlorhydria is always manifested. The amidulin reaction is present in all instances.

The *diagnosis* of larval hyperacidity does not usually present any difficulty. The symptoms of hyperacidity which arise early in the period of digestion, together with the characteristic features of the gastric contents, the large amount obtained consisting mainly of a watery secretion, with a low specific gravity, and with a normal acidity, and presenting the amidulin reaction distinguish this condition from the usual forms of hyperchlorhydria. The absence of an epigastric painful area, as well as the absence of occult blood in the stools, distinguishes it from gastric ulcer. Larval hyperacidity is differentiated from digestive or alimentary hypersecretion of gastric juice, with which it has many symptoms in common, by the presence of a hyperacidity during the early period of digestion, but which tends to become normal at that period when test meals are ordinarily withdrawn. The *treatment* should be largely directed toward the management of the nervous system. In emaciated individuals the best results are obtained by means of a systematic rest-cure treatment. The diet should consist largely of three meals a day, together with intermediate feedings of liquid food. The dietary should contain an excess of proteins and fats, and but a moderate quantity of carbohydrates. Of the various protein foods, milk, eggs, and fish are to be preferred.

Fats have a tendency to decrease the gastric hyperacidity, and are to be recommended. Of these, butter, cream, and olive oil are especially useful. The carbohydrates are only permissible in the most digestible forms, and vegetables should be mashed and strained and taken in the purée form, free of all cellulose. Water is usually well borne, and may be administered in large quantities, with benefit. All acid food, as well as stimulants, should be avoided. The alkalis, together with belladonna, are of great service. Good results are usually obtained from the use of hydropathic measures, as well as from massage.

### GASTROSUCCORRHŒA OR HYPERSECRETION OF GASTRIC JUICE

This is a condition in which a constant excessive flow of gastric juice is secreted. The stomach pours out this secretion even when free from food, so that large quantities of gastric juice may be found even in the morning before the ingestion of any nourishment. This disease was first described by Reichmann<sup>1</sup> in 1882, and afterward more fully elucidated by Riegel in various communications between 1884 and 1893.

<sup>1</sup> *Berl. klin. Wochenschrift*, 1882, No. 40.

The disease is found in three forms: gastrosuccorrhœa continua periodica, gastrosuccorrhœa continua chronica, and digestive gastrosuccorrhœa. There has been considerable diversity of opinion among various authors whether gastrosuccorrhœa should be placed in the category of organic diseases or among the neuroses. There is no question that in most instances this condition is a result of some marked organic gastric affection, as ulcer with obstruction, dilatation, or atony. On the other hand, in a small number of cases the condition can only be looked upon as neurotic; this is more frequently the case with the form known as gastrosuccorrhœa continua periodica than the continua chronica.

**Gastrosuccorrhœa Continua Periodica.**—By this is meant that condition in which, in addition to the appearance of the acute attacks with a constant secretion of gastric juice, severe gastric pains and vomiting are present. Rossbach<sup>1</sup> called attention to a condition which is closely related to periodical hypersecretion, but in which the attack takes its onset with violent headaches and which he terms gastroxynsis. Periodical hypersecretion may be present as a simple gastric neurosis or as a reflex neurosis, secondary to disease of the brain or spinal cord, *i. e.*, progressive paralysis, tabes dorsalis, or myelitis.

**Etiology.**—The causes are various, among which may be mentioned excessive mental strain, excitement, anger, overindulgence in food, and the abuse of tobacco. At times this condition is found in connection with the crises of locomotor ataxia, accounted for by the fact that the nerve fibres leading to the gastric glands regulating the flow of hydrochloric acid are unduly stimulated.

The patient suffering with this condition usually presents other nervous symptoms indicating the nervous origin of the disorder. The disease occurs usually in young people, and more frequently in males than in females. In a series of 1592 cases, 21 suffered with intermittent hypersecretion (1.5 per cent.).

**Symptoms.**—The characteristic signs of this condition are not only the paroxysmal appearance of the attacks, which take their onset in the midst of perfect health, but also the special character of the gastric contents and vomitus. The attack has its onset early in the morning, usually with lassitude, malaise, headache, loss of appetite, thirst, and pains in the stomach, which become intense and are accompanied by heartburn and acid belching. The pains become spasmodic and more intense, and finally vomiting sets in. The vomited matter is very acid, at first consisting of food and then of gastric juice: The attacks may thus be entirely recovered from, or after a short period of relief others may set in, extending over a period of from a few hours to several days. The vomiting can be prevented at times by the drinking of large draughts of water or by the administration of large doses of alkalis. The quantity of the vomited matter is usually very large in amount, often from 200 to 500 cc., containing at first food particles and afterward consisting of pure gastric juice, which is tinged yellowish or greenish with bile. The material first vomited is usually very acid, often containing 0.3 per

<sup>1</sup> *Deutsch. Archiv f. klin. Med.*, 1885, Band ccelvii.

cent. or more free hydrochloric acid, but afterward, when admixed with bile, the acidity is greatly reduced to or below normal. The vomited material may contain slight traces of blood, which has no special significance. During the attack, besides the intense pain there is a total loss of appetite, great thirst, and general feebleness; the pulse becomes weak and the patient presents the appearance of great suffering; he becomes pale and breaks out in a cold perspiration. The urine is greatly diminished in quantity and of a high specific gravity, while the bowels are constipated. The attacks vary greatly both as to intensity and duration, sometimes terminating gradually, sometimes suddenly. Between the attacks the patient is usually in good health, free of all disturbances, although at times moderate gastric disturbances exist, such as discomfort in the stomach, acid eructations and heartburn. Gastric analysis at this time usually reveals a hyperacidity, even though symptoms of hyperchlorhydria are not present. The condition known as gastroxynsis differs from periodic hypersecretion only in that the headache is a most important and persistent symptom. The other symptoms of gastroxynsis are so similar to those of periodic hypersecretion that these cases should be classed in the same category.

**Diagnosis.**—This is made by the appearance of the symptom-complex described, as well as by the finding of large quantities of gastric juice in the stomach at a time when no ingesta are present. The differential diagnosis must be made from periodic vomiting and the vomiting occurring in the gastric crises of locomotor ataxia. *Periodic hypersecretion* is distinguished from periodic vomiting by the irregular appearance of the attacks and by the vomiting of large quantities of pure gastric juice, whereas, in periodic vomiting, the attacks appear at regular intervals and the vomited material consists of mucus and bile. From the vomiting occurring in the gastric crises periodic hypersecretion is also differentiated by the appearance of large quantities of acid gastric secretion in the vomit and by the fact that the attacks persist during the night, neither of which is usual in the crises of locomotor ataxia.

**Prognosis.**—The duration varies greatly; some attacks are short, lasting but a few hours, others extend over a period of days. Sometimes the patient becomes greatly weakened and prostrated by the effect of the attack; in other instances his general health will in no way be impaired. If the primary cause can be determined and relieved the prognosis is favorable; on the other hand, this is impossible in many instances, and the attacks reappear at varying intervals.

**Treatment.**—This is, so far as possible, to seek out and relieve the cause. If due to overanxiety or mental strain, the patient should be ordered to the mountains or seashore. Physical exercises should be insisted on, and overindulgence in food and drink and in the use of tobacco prohibited. Hydrotherapy exerts a favorable influence.

In a number of our cases relief was afforded by means of intragastric electricity. In those instances in which the attacks have their origin from a hyperchlorhydria this condition must be treated. For the attack itself the mode of treatment advised by Einhorn<sup>1</sup> is often found service-

<sup>1</sup> *Diseases of the Stomach*, fourth edition, p. 362.



able; that is, to administer a moderate dose of bromide just as the attack begins; this method will at times abort an attack. As soon as the attack sets in the stomach should be thoroughly washed out with an alkaline solution, and this may be repeated a number of times during the attack. For the severe pain one is often forced to administer morphine hypodermically, this being the only remedy to be relied upon at times to produce even temporary relief. During the attack the patient should be allowed but small quantities of fluids, water, milk, and egg-albumen; bits of ice may be administered to relieve the thirst; also enemata of normal salt solution may be given.

**Gastrosuccorrhœa Continua Chronica.**—This is also known as Reichmann's disease, or chronic hypersecretion, and also as chronic continuous secretion of gastric juice. It is characterized by a chronic continuous secretion of gastric juice, even in the absence of food in the stomach, that is in the fasting stomach. This condition may be primary or secondary. It is primary when it occurs as a gastric neurosis independent of any known anatomical change in the stomach; it is secondary when it occurs as the result of some other gastric disturbance, such as ulcer, dilatation, or atony. As continuous hypersecretion is most frequently associated with dilatation, and as the symptoms of both conditions are very similar, many authors deny the existence of this condition as a separate entity and believe that it is simply a form of dilatation. It cannot be denied that most cases are secondary to dilatation.

The difficulty in differentiating between continuous hypersecretion and dilatation is more evident when we observe that of the six cases of this disease originally reported by Reichmann,<sup>1</sup> but one can be counted a case of chronic hypersecretion, the remainder presenting symptoms of hypersecretion secondary to pyloric stenosis. Riegel believes that continuous hypersecretion is in some instances a perversion of function and really of a neurotic type, in which no organic lesion can be detected. M. Pickardt<sup>2</sup> has reported three cases in which this condition was primary and existed as a pure neurosis, and in which careful investigation failed to present any organic disease of the stomach or motor insufficiency.

**Etiology.**—The causes are much like those of intermittent gastrosuccorrhœa, namely, great mental anxiety and excitement, indiscretion in the use of food, and the abuse of drink extending over long periods of time. Secondary continuous hypersecretion may arise as a result of dilatation, atony, or ulcer. Primary continuous hypersecretion is a rare disease; it does not occur as frequently as intermittent hypersecretion. In this series of 1592 cases there were 10 cases of primary continuous hypersecretion (0.63 per cent.), 7 in males and 3 in females; 4 were between twenty and thirty years of age, 3 between thirty and forty, and 3 between forty and fifty.

**Pathology.**—The anatomical changes in these conditions are not always uniform. Korezynski and Jaworski,<sup>3</sup> who investigated the subject most carefully, find no anatomical changes whatever in a certain

<sup>1</sup> *Berliner klin. Wochenschrift*, 1882, No. 40; 1884, Nr. 48; 1887, Nr. 12.

<sup>2</sup> *Ibid.*, October 30, 1905.

<sup>3</sup> *Deut. Archiv f. klin. Med.*, vol. xlvii.



number of cases. In others a special form of gastritis existed, associated with a degeneration and destruction of the peptic cells, while the parietal cells remained normal. Interstitial changes were also observed.

**Symptoms.**—The subjective symptoms of chronic hypersecretion are pain, burning in the epigastrium, heartburn, acid eructations, nausea, vomiting of large quantities of gastric juice, and increased thirst. These make their appearance gradually, and many patients complain of mild dyspeptic symptoms for years before the true nature of the disease is revealed. At first there is but a slight degree of burning in the epigastrium and heartburn, which gradually intensifies, then pain appears, coming on several hours after meals which is relieved by the ingestion of food. The pain also appears in attacks during the night, a rather characteristic symptom. After the pain has existed for some time, vomiting sets in, the vomitus consisting of a large quantity of a very acid gastric juice.

These symptoms may be mild in some patients and very severe in others; they are apt to appear for a certain length of time and disappear, to recur after weeks or months; in severe attacks the symptoms are present almost daily, and vomiting may occur four or five times a day. The patient loses flesh, the tongue and skin become dry, the appetite is increased in some cases, diminished in others. The attacks of pain can be often lessened by the ingestion of protein food, such as boiled eggs or milk. Constipation is usually present, and the quantity of urine is diminished, the chlorides decreased, and the phosphates increased. The objective signs consist in demonstrating hyperacidity as well as the presence of large amounts of gastric juice in the fasting stomach. The acidity of the gastric juice after a test breakfast may amount to 80, 90, 100, or more, and the free hydrochloric acid to 0.25 to 0.3 per cent. The protein digestion is good, showing a perfect peptone reaction, while the starch digestion is imperfect, the continuous flow of acid impeding amylolysis. The most important and characteristic symptom is the finding of gastric secretion in a fasting stomach; under normal conditions small quantities of gastric juice may be found in the stomach, but when quantities of 100 cc. or more are present the condition of hypersecretion must be considered, and especially so if it is discovered at a number of examinations. Even with smaller quantities than 100 cc. providing the other symptoms are present, such cases must be classified under the head of chronic continuous gastrosuccorrhœa.

In order to arrive at a more certain diagnosis, lavage should be given the evening before; the next morning the stomach is tested, fasting, so that no portions of former meals may be retained. The gastric secretion obtained from the fasting stomach is usually watery and often contains a small trace of bile; it is of a high total acidity and contains an excess of free hydrochloric acid, the peptone reaction being good, the dextrin reaction absent. In the secondary form of gastrosuccorrhœa continua chronica, dilatation or atony of the stomach is usually present.

**Sequelæ.**—Of the sequelæ or complications, atony and dilatation of the stomach, with or without ulcer, are the most common. Atony and dilatation often appear after the gastrosuccorrhœa has existed for a

considerable period of time; it is only in the earlier stages that the primary nature of the chronic hypersecretion can be determined; when the patient is seen late in the course of the disease, when both conditions are marked, it is often impossible to determine which is primary.

**Diagnosis.**—This is suggested by the symptoms, *i. e.*, excessive pain occurring several hours after meals and also during the night, with vomiting of large quantities of gastric juice. In addition there is burning in the epigastrium, heartburn, acid eructations, and increased thirst. The diagnosis is made certain by examining the stomach in the fasting state, when large quantities of gastric juice, usually over 100 cc., are obtained, showing an entire absence of amylolysis. It is important to practise lavage on the evening before the morning that the fasting stomach is tested. It is often important to exclude atony and dilatation, which, however, are often associated with gastrosuccorrhœa. In atony a motor insufficiency is observed, while in dilatation the motor insufficiency is so great that food particles are still present in the fasting stomach. This is not the case in gastrosuccorrhœa unless the condition is accompanied by dilatation. Ulcer will be excluded by the absence of occult blood in the feces and of a circumscribed painful area, and the presence of large quantities of gastric juice in the fasting stomach.

**Prognosis.**—This depends largely upon whether the condition is primary or secondary. If it is secondary to a dilatation, the prognosis is not as favorable as if it were primary, unless some radical procedure is undertaken, such as a pyloroplasty or gastro-enterostomy. When primary, the prognosis is usually not unfavorable, especially if rational treatment is undertaken. Frequent relapses are common, while certain severe cases are often very protracted and may continue indefinitely, notwithstanding the most rigid form of treatment.

**Treatment.**—This consists in relieving the irritation of the gastric mucosa and thus diminishing the flow of gastric secretion. Diet is of primary importance and should consist of small but frequent meals, given at intervals of from three to four hours. The patient should be required to eat slowly and masticate his food thoroughly; all irritating substances such as pepper, mustard, onions, and highly seasoned foods should be interdicted. As motor disturbances are apt to occur in this condition, fluids should be administered sparingly. The diet should be made up mainly of proteins, since these foods are well borne. The carbohydrates are poorly digested, and hence must be given only in small quantities and in the most easily digestible forms. All forms of meat are allowable, roast beef, lamb chops, chicken, and broiled steak, but should be finely minced. Of the carbohydrates the best are oatmeal, zwieback, Nestlé's food; purée of potatoes, spinach, etc., may also be allowed. Fats may be permitted to a greater or less degree in the form of good butter, cream, or olive oil. Milk is excellent, and may be taken either alone or mixed with small quantities of tea, coffee, or cocoa. It may also be given with eggs. The foregoing regulations as to diet apply to chronic hypersecretion without dilatation; when ectasia exists the dietetic rules described under this head must be followed.

Lavage of the stomach is a most efficient means of relieving pain and

irritation. This is best practised in the morning before the ingestion of food. Instead of lavage Boas recommends emptying the stomach in the fasting state (expression) by means of the tube; while Reichmann believes in lavage of the stomach with solutions of nitrate of silver 1 or 2 to 1000. Penzoldt advises douching with a solution of boric acid, and Einhorn sprays the stomach with nitrate of silver.

The alkalis play a most important rôle in the treatment of the disease; of these, bicarbonate of soda, calcined magnesia, phosphate and citrate of soda are most commonly employed. These are best administered two or three hours after meals, *i. e.*, at the height of digestion. Other remedies which are useful at times are bismuth subnitrate, given in large doses (half a dram), belladonna, and nitrate of silver in solution. Einhorn recommends the use of direct galvanization of the stomach.

**Digestive Gastrosuccorrhœa.**—Straus<sup>1</sup> first pointed out that in certain cases of hyperacidity relatively large quantities of a thin, watery, gastric secretion were obtained one hour after a test breakfast. He called this condition digestive or alimentary hypersecretion. Zweig and Calvo<sup>2</sup> investigated this subject more fully, and discovered that the large amounts of contents obtained after the test breakfast do not depend upon motor disturbances of the stomach, such as atony, but rather upon increased gastric secretion. Elsner<sup>3</sup> and Friedenwald<sup>4</sup> have also called attention to this condition. Boas<sup>5</sup> has investigated this question, and considers the name digestive gastrosuccorrhœa more appropriate than alimentary gastrosuccorrhœa, because the increased gastric secretion is dependent upon the act of digestion in contradistinction to continuous hypersecretion. In the latter the secretion extends beyond the digestive act, and more or less gastric juice is found in the fasting stomach.

**Etiology.**—This disease occurs most frequently in males. The 12 cases of Boas all occurred in males. In our 14 cases there were 12 males and 2 females, the ages varying between eighteen and sixty-four years.

**Symptoms.**—An important symptom is extreme emaciation, a loss of from ten to fifteen pounds being not unusual. This loss of flesh is a most important sign, especially since it appears without the slightest tendency to any disturbance of motility of the stomach. The appetite and quantity of food taken may be normal; occasionally, however, both may be decreased. The great loss in weight must be dependent upon the loss of gastric secretion. Amylolysis is extensively diminished and constipation very marked. The subjective signs are of much the same character as those found in nervous dyspepsia. Patients complain of various sensations in the stomach, pressure, fulness, eructations, excessive flow of saliva; occasionally violent pains; very rarely, if ever, heartburn. Nausea or vomiting occurs exceptionally. Marked splashing is observed in the region of the stomach; tender spots painful to pressure are, however, not observed; the abdomen is occasionally distended with

<sup>1</sup> *Deut. Archiv f. klin. Med.*, Bd. lvi, S. 120.

<sup>2</sup> *Archiv f. Verd.*, Bd. ix, S. 262.

<sup>3</sup> *Berlin. klin. Wochenschrift*, 1904, Nr. 25.

<sup>4</sup> *Am. Jour. Med. Sci.*, 1910, cxi, 318.

<sup>5</sup> *Deut. med. Wochenschrift*, 1907, Nr. 33, S. 135.



gas. A diminution in the chlorides and an increase in indican are frequently observed in the urine. This disease is much like atony, and Boas believes that there can be no question but that it has in many instances been mistaken for atony or nervous dyspepsia. In order to determine the presence of this condition, Boas advises a dry test meal. Inasmuch as bread contains 35.5 per cent. of water, he uses Albert cakes containing but 8.9 per cent. of water. If five Albert cakes are given as a test meal and removed from the stomach at the end of an hour under normal conditions, but a small residue will be obtained. In digestive gastrosuccorrhœa, however, 100 to 200 cc. of fluid will be obtained. On standing it forms into two layers, a lower layer slight in amount precipitated to the bottom, and above it a clear or slightly cloudy fluid three or four times as large in amount. The secretion generally shows a total acidity and percentage of free hydrochloric acid, usually not above and often below normal.

In a large proportion of our cases the total acidity varied from 40 to 56 and free hydrochloric acid 35 to 45, which indicates that while in this condition there may be no excess in the acids of the gastric secretion, the secretion is greatly increased in quantity. In other words, there is a hypersecretion but no hyperacidity. The average specific gravity of the gastric juice is 1.006. The secretion presents a more or less marked biuret and sugar reaction, while albumin is not present; erythroextrin, amidulin, and also the amylum reactions are usually marked. By means of the dry diet the diagnosis is made positive. If the bottom layer of the secretion is large, there must be a motor disturbance present.

**Diagnosis.**—The symptoms do not wholly point to the condition; the most marked ones are those of chronic nervous dyspepsia with marked emaciation, succussion in the region of the stomach a considerable period of time after meals and after small meals. The symptoms often point to atony, therefore, in order to make an exact diagnosis, three forms of examinations must be used:

I. Examination of the fasting stomach.

II. Examination of the gastric contents one hour after the dry test meal.

III. Examination of the gastric contents one hour after a test breakfast.

**Prognosis.**—This is not unfavorable. Alimentary gastrosuccorrhœa is a gastric affection of nervous origin, which is apt to extend over a long period of time, presenting great variability of symptoms, and with days and weeks of apparent perfect health giving place suddenly to periods of severe distress. That this disorder is purely a form of gastric neurasthenia is manifested by the fact that when the patient is restored to good health the increased secretion is apt to disappear.

**Treatment.**—The therapeutic indications are to increase the body weight, to avoid foods that increase the quantity of gastric secretion, and, finally, to counteract the imperfect starchy digestion, all three indications being corrected by the diet. It is also necessary to overcome the constipation, and this can be accomplished by the same means, namely, by a protein, fat and sugar diet, with a small proportion of carbohydrate. In place of sugar, dextrinized food can be utilized as

bread; the crust of wheat bread is to be preferred. Fluids should be given plentifully in order to avoid the irritation of the gastric juice upon the mucous membrane of the stomach. Alkaline drinks should be taken plentifully during meals. Soups, alcohol, black coffee, and tea should be avoided. Excellent results are obtained by a rest cure of some weeks. Of medicinal remedies, belladonna or atropine may be utilized; on the other hand, alkalis are most beneficial.

### GASTROMYXORRHŒA

By gastromyxorrhœa is meant a flow of mucus from the stomach. While various observers as Ewald, Riegel, Martius, have shown that small quantities of mucus were occasionally found in the fasting stomach, but little attention was paid to this condition until Dauber<sup>1</sup> pointed out that under abnormal conditions considerable quantities of mucus were secreted by the stomach and found in the fasting state. He called the disease chronic hypersecretion of mucus or gastrosuccorrhœa mucosa. Kuttner<sup>2</sup> investigated the subject farther, and found that the condition exists not infrequently, and is often observed in certain patients if lavage is practised on the fasting stomach. Friedenwald<sup>3</sup> reported 12 cases. The appearance of small quantities of mucus in the fasting stomach may be regarded as normal; it is important, therefore, to fix a limit to the quantity to be considered normal, and any amount beyond this must be looked upon as pathological. Kuttner regards the recovery of more than 5 cc. of mucus from the fasting stomach pathological, but considers the condition one of gastromyxorrhœa when more than 25 cc. are obtained. The condition can only be considered present if the secretion of mucus is constant or reappears at certain intervals. It is important, however, to consider the method by which the mucus is obtained. The patient should be accustomed to the use of the tube, as otherwise the mixture of saliva with the mucus will be so great as to vitiate the results. The method of moving the tube to and fro to induce the expulsion of mucus and the long continuance of the examination will increase the quantity of mucus. In order to arrive at a definite decision that there is an abnormal secretion, repeated examinations should be made. It is perfectly possible, too, that by swallowing saliva and pharyngeal mucus, secretion in the stomach may be excited; on the other hand, there must be a pathological disposition to secrete mucus in such cases, as the mucous membrane of the stomach would hardly react thus to so slight an irritation. Kuttner concludes that an increased secretion of mucus occurs in the fasting stomach, in gastromyxorrhœa.

**Intermittent Gastromyxorrhœa.**—This occurs rarely. Many cases are probably not recognized, as the discomfort is not lasting and the attention of the physician is not called to the condition. In this the increased secretion of mucus occurs at irregular intervals.

<sup>1</sup> *Archiv f. Verdauungskr.*, Bd. ii, S 167.

<sup>2</sup> *Berlin. klin. Wochenschrift*, October 30, 1905.

<sup>3</sup> *Boston Med. and Surg. Jour.*, 1908.

**Etiology.**—Kuttner was unable to find any evidences of locomotor ataxia in the patients whom he investigated. In 2 the attack took its onset with disturbances in the secretions of the nose. He believes, therefore, that there is connection between the affection of the nose and that of the stomach; the mucus of the stomach, however, is not simply swallowed, but in large part due to secretion.

**Symptoms.**—The attack may begin with prodromal symptoms, headache, loss of appetite, nausea, etc., but more usually in the midst of perfect health, often early in the morning, soon after awakening. The most striking symptoms of this paroxysmal attack is severe vomiting, which is intractable in the true sense of the word, as it cannot be successfully checked by any remedy. The vomited matter consists of large quantities of tough, slimy liquid, finally of bile and intestinal juices, but contains no food remains. Pain in the region of the stomach is not present, or if so it is of no moment. During the attack the stomach refuses to retain food, drink, or medicine. The patient feels wretched, the abdomen is retracted, the pulse small, the tongue dry, and the quantity of urine much diminished. The attack may extend over a period of one day, or may continue from three to five or even twelve days. The attack usually ceases quite suddenly, and after the cessation of the vomiting the patient can again take food without any annoyance. The patient enjoys good health during the interval of the attacks, and often has no or slight dyspeptic symptoms. The gastric contents after a test breakfast in the interval generally show a normal percentage of hydrochloric acid and only a slight amount of mucus.

**Treatment.**—A distinction must be made between the attack and the patient's general condition. In the beginning of the attack thorough lavage may terminate the symptoms at once, although when they are at their height lavage is valueless, and but little is to be gained by the internal administration of medicine. A hypodermic injection of morphine with atropine is sometimes useful. A condition of collapse accompanying a severe attack may be so serious, especially in patients with a weak heart, as to demand subcutaneous injections of camphor, enemata of normal salt solution, or a subcutaneous infusion. Treatment of the underlying condition is mainly directed to the removal of the neurotic tendency. At times a change of climate and atmosphere, hydrotherapy, massage, electricity, iron, and arsenic may produce a favorable influence upon the disease. Search should be made for a possible cause, either in the stomach itself or in other organs, such as the nose, and treatment should be directed to these conditions.

**Continuous Gastromyorrhœa.**—The chronic or continuous form is more frequent than the intermittent.

**Etiology.**—This condition may be associated with hypersecretion of acid or with various organic diseases, or may exist as an independent functional neurosis. Kuttner has found it associated most frequently with chronic catarrh, as well as with those nervous affections of the gastric mucosa in which there is a marked diminution or entire absence of hydrochloric acid. He also observed it in typical cases of gastric ulcer with or without pyloric obstruction. These diseases seem to be



rather favored by the ingestion of starchy food. The seat of origin of the mucus is not known, but it is probably a mixture of the secretion of the superficial epithelium and of the mucous glands, coming in largest measure from the glands of the pylorus.

It is impossible to determine whether this condition is always accompanied by a definite lesion of the mucous membrane, but as it is frequently associated with hypersecretion of acid, it may depend purely upon nervous influences. Twelve cases of this disease have come under the writer's observation,<sup>1</sup> nine in females, and only three in males.

**Symptoms.**—There are no characteristic symptoms, and the condition may be discovered in some cases in which there are no subjective symptoms. The diagnosis is established by the discovery of large quantities of mucus in the fasting stomach, shown to be the product of the gastric mucous membrane and not to come from other sources, such as the nose, mouth, or pharynx.

**Treatment.**—Lavage should be practised for the removal of the mucus, provided there is no contra-indication to the procedure; instead of this method of treatment, mineral waters may be utilized, being chosen with reference to the nature of the associated disease, the general condition of the patient, and the various gastric functions.

In contradistinction to gastromyorrhœa, Kaufmann<sup>2</sup> described a frequent finding in the gastric contents, that is a complete lack of mucus, which he terms amyxorrhœa gastrica. This may be due to different causes. Kaufmann calls attention to the fact that the mucus is a protective agent of the gastric mucosa, and that in some of the cases presenting symptoms of hyperacidity, and in which the stomach contents shows no excess of acid, but normal or even subnormal figures of acidity, the lack of sufficient mucus is the principal cause, rendering the mucosa hypersensitive even to secretions of a normal or moderate degree of acidity. The symptoms of hyperacidity disappear under treatment with nitrate of silver, which increases the amount of mucus.

## BULIMIA

Bulimia is that condition characterized by an abnormal increase in the sensation of hunger. It has also been termed hyperorexia, cynorexia, and lycorexia. Rosenthal believes this disorder is due to an excitation of the hunger centre, and this is probably true in cases of the affection following brain diseases. Stiller considers it due to irritation of the peripheral nerve endings in the stomach itself. It is probable that there are some forms due to lesions of the brain, while others are due to excitation of the nerves in the stomach itself. It has been stated that the sensation of hunger is due to stimulation of the hunger centre in the medulla by blood impoverished in the nutritive substances, and that this condition is overcome when the nutritive value of the blood is increased. That this will not entirely account for the sensation is shown by the statement that the appetite is satisfied as soon as the

<sup>1</sup> *Boston Med. and Surg. Jour.*, 1908.

<sup>2</sup> *Am. Jour. Med. Sci.*, 1908, cxxxv, p. 207.

stomach is filled with food, long before the nutritive material has reached the centres of the brain. On the other hand, Leo has stated that increased appetite is due to the rapid evacuation of the stomach, which must be accompanied by a pyloric insufficiency; yet Ewald and Fleischer have observed cases in which an increased motility of the stomach did not exist. Recently, Cannon has advanced the theory that the sensation of hunger is produced by tonic contractions of the empty stomach.

**Etiology.**—Bulimia may exist as a primary neurosis or may be secondary to diseases of the stomach or other organs. As a primary neurosis, it is found in neurasthenia and hysteria. It occurs in cerebral tumors, Basedow's disease, pulmonary tuberculosis, diabetes, syphilis, intestinal worms, in ulcer and dilatation of the stomach, and in many other conditions. Bulimia is most frequently observed in females between the fifteenth and fortieth years. In the series of 1592 cases of gastric neuroses bulimia occurred in 24 cases (1.5 per cent.).

**Symptoms.**—This condition usually occurs in attacks at irregular intervals, although at times they may appear periodically and extend over a long period of time or may be of short duration and be followed by an attack of anorexia. The disorder comes on as a violent sensation of hunger occurring after meals, in consequence of which the patient becomes exhausted, feels faint, has gastric pains, ringing in the ears, and suffers with vertigo and cold extremities. This continues until some food is taken. A very small quantity of food will at times overcome the sensation for a longer or shorter period of time; occasionally very large quantities must be ingested to relieve the condition. In one case of this series a quantity of food representing 6250 calories was consumed daily. In consequence of the inordinate amount of food, other disturbances of digestion are apt to follow, such as atony, gastritis, and disturbances of the intestines. The gastric contents were examined in 21 of 24 cases; normal acidity was found in 15 (72 per cent.), hyperacidity in 3 (14 per cent.), and subacidity in 3 (14 per cent.); hypermotility was present in 6, normal motility in 12, and atony in 3 cases.

**Diagnosis.**—Bulimia must be differentiated from acoria and polyphagia. In bulimia there is an abnormal desire for food, but the desire can be satisfied, while in acoria there is an absence of the sensation of satiation. In polyphagia or gluttony, while the appetite remains good, the feeling of satisfaction is delayed to such an extent as to create a constant desire for more food.

**Prognosis.**—This depends upon the cause, whether it is primary or secondary to some other disorder. The primary form due to neurasthenia or hysteria may be protracted or may disappear suddenly; when secondary, the prognosis depends upon the nature of the primary disease.

**Treatment.**—In treatment special attention should be directed toward the primary disorder. In those forms due to neurasthenia and hysteria the nervous system in general should receive special attention. In many cases rest, change of scene, hydrotherapy, electricity, massage, and psychotherapy are effectual means of combating this condition. The diet should be carefully regulated. Patients should be required to eat slowly and masticate the food thoroughly. Nourishment should

be taken at frequent and regular intervals, such as every two hours. The food should consist largely of milk, eggs, cereals, boiled fish, the lighter meats, and green vegetables. Fried foods and sweets should be avoided. Intra-gastric galvanization has proved effectual in some cases, while at times the intra-gastric douche has been used with some success. The bromides have been used advantageously, the bromide of strontium in 15-grain (1 gm.) doses taken three or four times a day, being most useful. Arsenic, codeine, and opium have also been recommended.

### PAROREXIA

Parorexia is that condition characterized by a perversion of the appetite. According to the character of the perversion we have: (1) Pica, desire for articles which are not foods, such as chalk and earth. (2) Malacia, desire for spiced food, vinegar, mustard. (3) Allotriophagia, desire for disgusting substances, such as urine and fecal matter.

Pica and malacia are often observed in the same individual. Parorexia is found in neurasthenia and hysteria, occasionally in disturbances of the digestive tract, helminthiasis and gastralgia, and often in the insane. Malacia is frequently observed in chlorotic girls and pregnant women, while allotriophagia is found in the insane. In this series of 1592 cases there were 8 cases of parorexia (0.5 per cent.), 6 being in males and 2 in females; 3 were from ten to twenty, 2 from twenty to thirty, 2 from thirty to forty, and 1 from forty to fifty years of age.

### GASTRALGOKENOSIS (PAINFUL GASTRIC EMPTINESS)

Boas has introduced this term to indicate that neurosis characterized by the appearance of pain in the stomach, occurring when the stomach is empty, and which disappears as soon as food is taken. It may occur as a permanent neurosis, or come on periodically. According to Boas, this condition is produced by severe contractions of the pylorus, and is relieved when food is present in the stomach.

**Etiology.**—This condition is found in neurasthenic individuals who are subject to worry and anxiety, or who have been leading an irregular life. Examination of the gastric functions shows normal conditions both as to secretion and motility. This affection occurred only in males in 7 of this series (0.5 per cent.); of these, 3 were between twenty and thirty, 3 between thirty and forty, and 1 between forty and fifty years.

**Symptoms.**—The condition manifests itself by the appearance of pain, which at times becomes intense, from one to two hours after meals. An attack may appear during the day or night, and last from fifteen to thirty minutes. The pain is immediately relieved by taking food.

**Treatment.**—This consists in properly looking after the underlying neurasthenia. Patients should be taught not to allow the stomach to become empty, and for this reason should be encouraged to take food every two hours. Boas has obtained good results by the use of opium.



### GASTRALGIA NERVOSA

Gastralgia nervosa is the condition characterized by periodic or spasmodic attacks of pain in the stomach, appearing independently of the ingestion of food and not associated with any organic disease. The pains of a gastralgic type present in ulcer, cancer, dilatation, and in some forms of gastritis are accompanied by organic changes, and cannot be properly classified under the head of gastralgia nervosa.

**Etiology.**—Gastralgia is usually considered as a neurosis of the vagus, and only a marked increase in the condition to be described as gastric hyperesthesia. Einhorn divides gastralgias into five varieties: (1) Of gastric origin; (2) of central origin; (3) of neurotic origin; (4) of constitutional origin; and (5) of reflex origin.

1. Gastralgias of gastric origin. In this class are found the neuralgic pains present in cancer and ulcer of the stomach, in certain forms of gastritis, and produced by adhesions from the stomach to other organs.

2. Gastralgias of central origin. In this class are the attacks of pain observed in the gastric crises of locomotor ataxia, and the gastric pains in cerebral tumors and myelitis.

3. Gastralgias of neurotic origin. This is often observed in hysteria and neurasthenia, and usually simultaneously with other symptoms.

4. Gastralgias of constitutional origin. Gastralgia may be due to some change in the blood, as in lead-poisoning, anemia, and gout.

5. Gastralgias of reflex origin. This form is due to disease of other organs, as the generative system, and enteroptosis.

Gastralgia is more frequent in women than in men. In this series of 1592 cases of gastric neuroses, there were 24 cases of gastralgia (1.5 per cent.), 17 being in females and 7 in males.

**Symptoms.**—The attacks of pain, as a rule, appear suddenly; occasionally they are preceded by premonitory symptoms, such as fulness in the stomach, nausea, vomiting, and headache. The pain may be burning, boring, tearing, cutting, or gnawing, and is usually felt in the epigastrium; at times it radiates throughout the entire abdomen or even to the back, and may be so intense as to cause weakness and collapse, the patient having a thready and irregular pulse, with pallor, cold extremities, and cold perspiration. Often the pains are relieved by pressure; at times these symptoms are accompanied by nausea, vomiting, and hysterical manifestations, such as globus hystericus and nervous chills. The duration varies, the attacks may last from a few moments to many hours, and the intervals between may be days, weeks, or months. In the gastric crises of locomotor ataxia the attacks of gastralgia are usually ushered in with pains in the legs and arms, nausea and vomiting. These crises may precede the classic signs of locomotor ataxia by months or years. Boas calls special attention to the gastralgic pains occurring in neurasthenic females at the menstrual period.

In most instances this condition bears no relation whatever to the character of the food taken. The pains begin in the epigastrium, remain localized, and are burning and boring in character. The attacks last from fifteen to thirty minutes, and are repeated several times during

the day, while at night the pain is absent. Another form is that produced by open inguinal or femoral rings, occasioning small or occult hernia, also by hernia of the abdominal walls. These are observed most frequently along the linea alba. The pain is colicky, and ceases when the patient reclines. Neurasthenic symptoms are almost always present.

**Diagnosis.**—This is made by the character of the attacks with paroxysmal pain, bearing no relation to the ingestion of food, and at the same time not associated with any organic or other functional disease of the stomach. As gastralgia is usually due to some other condition, care should be taken to determine as far as possible its etiological relation. Gastralgia must be differentiated from ulcer. In *ulcer* there is a circumscribed painful area in the epigastrium and in the back to the left of the eleventh or twelfth dorsal vertebra. The pain is proportionate to the quality and quantity of food ingested, and is accompanied by nausea and vomiting; is relieved by vomiting; occult blood is found in the feces at times. When there is still doubt Leube recommends the ulcer rest cure in order to determine from the result of the treatment the presence or absence of ulcer. Gastralgia is differentiated from *chronic gastritis* by the slower appearance of the pains after the ingestion of food, by the presence of the paroxysms of pain, and by the absence of any change in the gastric secretion. It is differentiated from *cancer* by the absence of the usual signs; the pain usually not being paroxysmal in cancer. Intestinal *colic* may be mistaken for gastralgia, but in it the intestine is inflated with gas, and the pain is relieved by the passing of gas or a movement of the bowels, which frequently contains mucus. The pain of intestinal colic changes its position, while in gastralgia it is localized, as a rule, in one area. Intercostal *neuralgia* is distinguished from gastralgia by the fact that in the former condition the intercostal area is painful to pressure along the course of the nerve. *Gall-stone attacks* may be mistaken for gastralgia. In these the pain is generally to the right of the median line, the attack is accompanied by fever, and there is often a sensitiveness of the liver. In some cases the diagnosis is most difficult, especially when the more important symptoms of cholelithiasis are absent. *Nephritic colic* is differentiated from gastralgia by examination of the urine. The pain in nephritic colic radiates toward the bladder.

**Treatment.**—It is important to direct our attention to the underlying cause. The form due to anemia should be treated with iron and arsenic; that due to malaria by means of quinine; and that from nicotine poisoning by cautioning against the use of tobacco. Reflex gastralgia must be handled by treating the primary disease. That due to neurasthenia and hysteria should be treated by change of scene, rest, electricity, and massage. In patients much run down a systematic rest cure will produce excellent results. The attacks of pain are treated as follows: hot applications in the shape of a hot-water bag or hot poultices or packs are placed on the abdomen and the patient given half a grain (0.03 gm.) of codeine or 20 to 30 drops (1.5 cc.) of Hoffman's anodyne. Belladonna and chloroform water have also been recommended, as well as phenacetin and antifebrin. If the attacks of pain are intense, a

hypodermic injection of morphine must be administered or opium and belladonna given by rectum. The galvanic current is of considerable value, the anode being placed on the epigastrium and the cathode on the spinal column. Strong currents are used. At times better results may be obtained by means of intragastric galvanization.

### HYPERESTHESIA GASTRICA

By gastric hyperesthesia is meant that condition in which the mucous membrane of the stomach is unduly sensitive, even to its normal contents. The lightest forms of foods will often cause distress in spite of the fact that the stomach presents neither secretory nor motor disturbances. The character of the discomfort may be pain, fullness, burning, or sensations of cold occurring after meals. In some instances, not only does the food cause discomfort, but the normal amount of hydrochloric acid will cause pain, similar to that found in hyperacidity, and it may exist even when the acid is diminished or absent.

Under the subjects of achylia gastrica and hyperchlorhydria, it was shown that symptoms of hyperacidity occasionally exist in achylia gastrica; in these cases there is evidently a hyperesthesia of the gastric mucous membrane, which is so sensitive that it cannot tolerate even the normal amount of acid. Again, a condition is often observed in which the percentage of acid may be far in excess of normal, and yet the individual have perfect health without gastric disturbances.

**Etiology.**—As a primary affection, hyperesthesia is found in neurasthenia and hysteria, and frequently in anemic females; it occurs secondary to affections of various organs, such as ulcer of the stomach, chronic gastritis, and disease of the kidneys (uremia). It may be produced by excesses in food and drink, the abuse of coffee, tea, alcohol, indulgence in highly seasoned food and tobacco, or it may come from drug habits, such as opium or cocaine. The taking of sufficient food, fasting, living on an exclusive diet, or eating irregularly are also etiological factors. Hyperesthesia is the affection from which conditions such as anorexia nervosa, nervous nausea and vomiting, gastralgia, and sitophobia often take their origin. In this series of 1592 cases there were 31 cases of hyperesthesia (2 per cent.).

**Symptoms.**—The sensation produced is that of mild pain, fullness, and burning, appearing soon after meals and continuing during digestion, and ceasing when the stomach is empty. In some cases the pain is greater, and may cause nausea and vomiting. The disturbance is often greater from liquid than from solid food. On account of the discomfort produced, much food is discarded and the patient emaciates and loses strength. Some of the cases manifest the symptoms of hyperchlorhydria, notwithstanding that the acidity may be normal or subnormal. In these cases the discomfort appears several hours after meals and disappears on the ingestion of food or the taking of alkalis. On palpation the whole gastric area may be sensitive to pressure but free from localized painful points. The gastric secretion shows a normal percentage of



free acid, with occasional slight variations. The motor function of the stomach is not disturbed.

**Diagnosis.**—This is usually made with ease, provided the symptoms above described are present together with a normal gastric secretion. Hyperesthesia must be differentiated from ulcer and chronic gastritis. In ulcer there is a localized painful area and the pain is proportionate to the quality and quantity of food ingested. In chronic gastritis there is usually a diminution of gastric secretion, together with the presence of mucus, while the symptoms of distress do not appear immediately after meals, but some time later.

**Treatment.**—In all instances the patient should be required to remain in bed, at first on a milk or egg-albumen diet, and, if possible, combined with a systematic rest cure, the food being increased gradually until solid food is taken. In serious cases, rectal alimentation must be practised for a few days at the onset. Cold compresses should be applied to the abdomen. Galvanization is efficacious in some cases. Nitrate of silver may be given by mouth, grain  $\frac{1}{8}$  (gm. 0.008) in solution, three times daily, or administered by means of the stomach douche. At times the bromides, valerianates, and sumbul prove useful, especially in those forms due to neurasthenia and hysteria to which attention must always be directed. In the cases dependent upon anemia, iron is indicated.

**Gastric Idiosyncrasies and Abnormal Sensations.**—There are certain individuals who manifest an idiosyncrasy toward certain foods which when taken produce gastro-intestinal disturbances or some eruption on the skin. Among the foods causing this class of symptoms are fish, berries, cheese, etc. Fever, headache, gastric pain, nausea, vomiting, and urticaria are accompanying symptoms. The writer has constantly noticed the condition in a certain patient after eating eggs. The only means of preventing it is to order the individual to abstain from the food that causes this discomfort. There are abnormal sensations met with in neurotic individuals, such as cold, heat (stomach burn), epigastric pulsations, constrictions, and sensations of a foreign body in the stomach. The gastric secretion is normal in all these instances, and there are usually other neurasthenic symptoms present that indicate the nature of the disorder. The treatment must be directed to the nervous system in general. The bromides and belladonna are at times of value.

### MERYCISM OR RUMINATION

By merycism is meant that condition in which there is a regurgitation of food into the mouth which is again masticated and then either reswallowed or spat out. This act is accompanied by a more or less pleasurable sensation and without nausea or effort, and occurs some time after meals. Rumination in man is comparable to the same condition found in certain animals. Some authorities attribute this disorder to a paresis of the cardia, while others consider it a reflex neurosis causing a temporary relaxation of the cardia. Rosenthal holds it is due to an irritation of the vagus, producing an opening of the cardia through Openchowski's dilator fibres, occasioning an antiperistalsis of the

œsophagus. There are two classes of phenomena aiding in the production of the disorder, one active, the other passive; the active consists in depression of the diaphragm and contraction of the muscles of the abdomen, both of which produce a void in the thoracic cavity; and contraction of the abdominal muscles which compress the stomach. "The passive phenomenon consists in the elongation and widening of the œsophagus and the diminution of the lumen of the stomach" (Spivak).

**Etiology.**—Heredity plays a rôle in a number of cases which have been reported. The writer has observed the condition in a father aged fifty-one and a daughter aged fourteen years. In many cases other neurotic and hysterical tendencies have been observed. At times the condition is acquired by imitation.

Among the causes to which rumination is said to be due are rapid eating, worry, fear, nervous strain, and sudden shock. A large number of cases occur among idiots and the insane. The disease is observed more frequently among men than women. It is found at all ages, and is most common in highly intellectual men. In the series of 1592 cases of gastric neuroses there were 24 cases of *merycism* (1.5 per cent.). Among them were five students, one artist, two lawyers, three physicians, five clergymen, two merchants, one baker, and one mechanic. The gastric contents were examined in 19 of the 24 cases of this series; a normal acidity existed in 11, hyperacidity in 3; subacidity in 2; anacidity in 1; and heterochylia in 2 cases. Atony was found in 3 cases, while in the others the motor function was normal.

**Symptoms.**—Rumination usually begins as a voluntary process in an insidious manner; on account of gastric discomfort the food is first regurgitated, producing a pleasurable sensation it is again reswallowed, and finally the condition of *merycism* is established as an involuntary process. The regurgitation usually takes place during the early period of gastric digestion; it rarely occurs in the fasting stomach; the remastication continues as long as the regurgitated food has a pleasant taste; as soon, however, as it becomes acid (during the late period of digestion) it is either swallowed at once or ejected. Rumination may take place after every meal and last for a very short period of time or extend over hours. *Merycism* occurs alone or may accompany other gastric disorders; it is occasionally associated with atony and dilatation of the stomach. As a rule, the general nutrition of patients suffering with this disorder is good; although when large portions of all meals are not reswallowed emaciation is produced and the general nutrition affected.

**Diagnosis.**—This is made without difficulty. It differs from regurgitation in that the food is again masticated, while in the latter this process does not take place. In vomiting, nausea and retching are present, while *merycism* is accompanied by pleasurable sensations.

**Prognosis.**—This is often good, especially if the patient makes the effort to overcome the habit. This condition may extend over a long period of time, being present occasionally during the entire life, or it frequently disappears for a period, to recur following some strain or shock.

**Treatment.**—This consists essentially in an autosuppression. In a certain number of cases the patient can be taught to overcome this

disease. He should be required to eat slowly and masticate thoroughly; 3 patients of this series were cured in this way. The state of the gastric secretion occasionally gives a clue as to treatment. Hydrochloric acid is useful in cases of subacidity while alkalis are of benefit in superacidity. Intra-gastric electricity has been recommended, and was of great benefit in 2 patients. In those who are much run down and weakened by disease a thoroughly regulated rest cure with psychotherapy is most effective; 3 patients were cured in this way. Strychnine and quinine have been recommended, inasmuch as their taste destroys the desire to remasticate. Lavage has been used by Johannessen and gavage by Jurgensen.

### REGURGITATION

By regurgitation is meant that condition observed in hysterical and nervous individuals when food is brought up in small quantities from the stomach into the mouth and usually ejected. This disorder is much like rumination, except that food is not remasticated; rumination, however, may develop from long-continued regurgitation.

**Etiology.**—This is the same as that of rumination. The condition is usually found in neurasthenic and hysterical individuals, and is at times voluntary; however, as the habit becomes established it becomes involuntary. Regurgitation may be occasioned by a nervous strain or shock, or may be secondary to some other gastric disturbance, such as dilatation, catarrh, or hyperchlorhydria. This disorder is also largely found in adult males, and more frequently in individuals pursuing intellectual pursuits. It occurs more frequently than rumination. In the series of 1592 cases of gastric neuroses it was present in 32 cases (2 per cent.), 26 being in males and 6 in females. Among those suffering from this affection, there were two artists, three students, three physicians, six lawyers, five ministers, four teachers, three merchants, one mechanic, and one laborer. The gastric secretion is usually normal. In the series of 32 cases the gastric contents were examined in 29, and normal acidity was found in 23 (79 per cent.), hyperacidity in 3 (10 per cent.), subacidity in 2 (8 per cent.), and heterochylia in 1 (3 per cent.). The motor function was usually normal, a slight atony existing in five.

**Symptoms.**—The onset is gradual, and consists in the regurgitation of food from the stomach soon after eating and persisting during the entire period of digestion. It is not preceded or accompanied by nausea, and if it occurs early in the process of digestion, the regurgitated material has the same taste as the food swallowed. Later it becomes sour from the mixture of the acid of the gastric juice. At times this process can be suppressed, at other times not. The food is not remasticated and swallowed with pleasure, as in the cases of rumination. Regurgitation may occur after any meal, or only after certain ones; it may disappear for a time, to recur after some mental strain or excitement. When large portions of all meals are habitually regurgitated and ejected, the general nutrition of the patient is likely to suffer.

**Diagnosis.**—Regurgitation is differentiated from vomiting by the absence of the usual signs of the latter, nausea, retching, salivation, etc.



It is distinguished from œsophageal regurgitation due to stenosis of the œsophagus by the presence of the gastric secretion in the regurgitated matter. The difficulty or inability to pass the tube in œsophageal stenosis aids in differentiating this from gastric regurgitation.

**Prognosis.**—This is usually favorable, provided the patient will assist in the act of suppression of the condition; the health becomes seriously affected only in those instances in which all food is constantly regurgitated.

**Treatment.**—The general condition should be looked into and the associated neurasthenia or hysteria treated. An important factor consists in teaching the patient voluntary suppression. In emaciated individuals this may be assisted by a rest cure with isolation. The patient should be required to eat slowly and masticate his food thoroughly. Intragastric electricity is valuable in some cases. Strychnine and the bromides have been used with good results.

### ERUCTATIO NERVOSA

Eructatio nervosa is a condition characterized by periodic or paroxysmal attacks of noisy belching; it occurs in neurasthenic and hysterical individuals. The question of the origin of the gas expelled has attracted much attention. The following sources have been suggested: The fermentation or putrefaction of food, causing the formation of gases, or the swallowing of air (aërophagia). It is now generally admitted that the gas which is expelled in eructatio nervosa is swallowed, and that the air passes into the stomach by an act of deglutition. The swallowing of small quantities of air is a natural phenomenon accompanying the deglutition of food. Aërophagia, on the other hand, occurs as a voluntary act, induced to relieve an uncomfortable sensation in the stomach or œsophagus by the expulsion of gas that has been swallowed. Convulsive deglutition is accompanied by forcing air into the œsophagus and stomach, while expulsion is occasioned by contraction of the œsophagus expelling the accumulated air with a loud characteristic sound. Oser<sup>1</sup> ascribes this condition to aspiration, air being suctioned in and expelled through the œsophagus by expansion and contraction of the stomach. Linossier believes that aërophagia is much like regurgitation, and that while in regurgitation there is an expulsion of food, in aërophagia there is an expulsion of gas. In some cases, as Ewald points out, the belching has no connection with the stomach, but originates from the œsophagus by contractions of the muscles of the neck.

**Etiology.**—Eructatio nervosa is usually found in hysterical or neurasthenic individuals. It is more common in females, and in younger than in older persons. In the series of 1592 cases of gastric neuroses there were 54 cases of eructatio nervosa (4 per cent.), 42 in females and 12 in males. While this condition is usually a simple gastric neurosis produced by some mental excitement, such as anger, worry, or great sorrow, yet it may occur as a result of some other gastric disturbance. Catarrh,

<sup>1</sup> *Die Neurosen des Magens*, 1885, S. 137.

gastroptosis, or a reflex condition secondary to disturbances of other organs, such as the genito-urinary organs and heart, may produce it.

**Symptoms.**—This disorder usually develops suddenly and is accompanied by noisy eructations, which vary in duration and intensity, the paroxysm lasting from a few hours to days. Frequently there is a period of quiescence between the paroxysms, the attack presenting no definite relation to the quality and quantity of food taken. The number of eructations varies greatly. Spivak<sup>1</sup> calls attention to two forms of nervous eructations, voluntary and involuntary. In the first variety the patient controls the condition, and is able to inhibit this habit at will; in the second, which generally occurs during an attack of hysteria, he is unable to do so. The attack is spasmodic in character and cannot be controlled. The paroxysm usually disappears suddenly and ceases during sleep. On examination, patients suffering with nervous eructations present a rather increased sensibility to pressure in the epigastric region. These areas on pressure occasion eructations (aërophagenic points, Bandouin). Examination of the gastric contents may or may not reveal normal conditions. In this series of 54 cases the gastric contents were examined in 51; normal acidity existed in 42 cases (82 per cent.), superacidity in 6 (12 per cent.), and subacidity in 3 (6 per cent.).

**Diagnosis.**—This is not usually difficult. The characteristic paroxysmal attacks can scarcely be mistaken. There is usually an absence of organic disease; the gastric contents are frequently normal (82 per cent. of this series); the gas expelled is atmospheric air and shows no signs of fermentation, while the examination usually reveals other neurasthenic or hysterical symptoms.

**Treatment.**—Mild forms of the disorder may be combated by explaining its nature to the patient and urging him to control the attack. Sometimes, however, this is difficult, and we must content ourselves with the treatment of the neurasthenic condition. This may be accomplished by hydrotherapeutic measures, electricity, and change of scene. In persons who are much run down and have lost much flesh nothing will accomplish such excellent results as a well-regulated rest cure. At times good results may be obtained by means of lavage, douching the stomach, or by means of intragastric electricity. Drugs are usually of little value. Among those employed in this condition with more or less effect are the bromides, chloral, codeine, and belladonna.

### NERVOUS VOMITING (VOMITUS NERVOSUS)

The act of vomiting is a very complicated process; not only does the nervous system play a part in the act, but also the muscles that govern the movements of the stomach. In addition to the centres governing the stomach movements there is a coördinated action of the vomiting centre from which this act takes its origin. The vomiting centre is in the medulla in the vagus nucleus in close proximity to the centres transmitting impulses to the muscles of the stomach, diaphragm, and pharynx.

<sup>1</sup> *New York Medical Record*, April 29, 1905.

**Etiology.**—Vomiting may be due to one of three conditions: to some abnormal state of the food, to some disease of the stomach itself, or to some disturbance of the nervous system. The form with which we are here concerned comes under the latter head. It may be divided into three groups: (1) Cerebrospinal vomiting due to a lesion or functional disturbance of the nervous centres. (2) Nervous vomiting proper, or vomiting due to neurasthenic or hysteria. (3) Reflex vomiting.

Stiller<sup>1</sup> points out the following features as characteristic of this form: (a) The ease of the vomiting. (b) Its non-dependence upon the quality and quantity of the ingested food. (c) The capriciousness with which very bizarre articles of food are retained to the exclusion of others. (d) The occasional elective vomiting that consists in selecting only one form of food which is separated from the chyme. (e) The ease with which patients bear this condition even for a long period of time. (f) The very slight degree of inanition produced by the habitual vomiting. (g) The extraordinary influence of the slightest external or internal causes that react on the patient's temperament. (h) The occurrence of vomiting frequently, even on a fasting stomach, and the appearance of this condition independently of the meal. (i) The presence of other nervous symptoms associated with the vomiting or alternating with it.

In this series of 1592 cases of gastric neuroses there were 49 of nervous vomiting (3 per cent.), 34 in females and 15 in males; as to age, 6 were in the first decade, 6 in the second, 14 in the third, 11 in the fourth 8 in the fifth, 3 in the sixth, and 1 in the seventh.

**1. Cerebrospinal Vomiting.**—The cause of this form (also known as central vomiting) is found in the brain, spinal cord, or the membranes covering these structures. The condition has been observed as a symptom of inflammatory disease of these structures. It is found in meningitis, encephalitis, apoplexy, abscess, cerebral tumors, not infrequently after brain anemia or hyperemia, concussion, intoxication from ether, chloroform, opium, tobacco, or septicemia and auto-intoxication. Spinal vomiting due to disease of the cord is rather infrequent; it occurs most commonly in the gastric crises of locomotor ataxia and occasionally in transverse myelitis. The *gastric crises* are characterized by the occurrence in the midst of well-being, of sudden attacks of intense pain appearing in the epigastrium radiating toward the sides and back. They are followed by the vomiting of large quantities of food, mucus, bile, and finally of intestinal juices and occasionally of blood. After copious vomiting temporary relief is afforded, and the attack ceases, especially during the night, to return on the following day. It may continue at intervals from six to eight days, or may last even longer. The vomiting may cease as suddenly as it appeared, the appetite may return, and the general condition of the patient improve.

During an attack the patient becomes weak and prostrated, the pulse is feeble and rapid, the appetite disappears, the bowels become constipated and the thirst intense, while the abdomen is much retracted. The examination of the vomited matter for free hydrochloric acid may

<sup>1</sup> *Die nervose Magenkrank*, 1884, S. 151.



reveal a normal, subnormal, or hyperacid secretion. The diagnosis of locomotor ataxia is made by the presence of the other characteristics of this disease, but inasmuch as gastric crises may occur as early symptoms of tabes, the diagnosis may be difficult.

**2. Nervous Vomiting Proper.**—This form of nervous vomiting is most frequently associated with neurasthenia or hysteria. It is found mainly in hysterical females; in this series it occurred in 19 females to 4 males. The vomiting is often accompanied by pains in the stomach, and comes on more or less frequently every day or every few days and is often observed after some severe mental strain or excitement. Nausea is frequently absent in these cases, the vomiting occurring without any effort whatever; other symptoms of neurasthenia or hysteria are either associated with the vomiting or alternate with it. The *diagnosis* of nervous vomiting is established by the presence of associated nervous symptoms, and by its non-dependence on the quantity and quality of food taken; further by its irregularity, the expulsion of either only solids, or only liquids, or only one particular form of food, or only a portion of the meal, and the very slight loss in strength and weight. In this condition the skin is usually dry; the quantity of urine excreted is small, with a marked diminution in urea. The vomiting may continue for days or months and then disappear suddenly without apparent cause.

*Periodical Vomiting.*—This condition was first described by von Leyden, and is characterized by vomiting occurring at regular intervals; between the attacks the patient is in normal health, and complains neither of gastric distress nor disturbance of the nervous system. The attacks come on abruptly and disappear as suddenly, lasting from a few hours to twelve or fourteen days, the attack as well as the interval having a constant and definite duration. The attack is usually ushered in abruptly by nausea, gastralgic pain, and headache, followed by vomiting, at first of gastric contents and mucus, and then of bile. The vomiting is excessive, no food, not even fluids, being retained by the stomach during this period. The patient becomes weakened and prostrated, the pulse weak, the tongue dry, severe, lancing pains often occur in the extremities, constipation becomes marked, and the urine is diminished. The vomiting ceases suddenly and the attack gradually passes off, to be repeated again at an interval of from two to four or six weeks or even several months. When the attacks occur at short intervals emaciation may be extreme, and the disease becomes most serious, in consequence of the extreme inanition produced. A distinctive feature is the typical periodicity by which it can be distinguished from the gastric crises of tabes. An examination of the stomach contents in these cases usually reveals normal conditions.

*Psychic Vomiting.*—This is generally due to some form of shock, fright, or sudden mishap. It may be mild or intense. In mild forms only portions of the food are vomited for a certain period of time, and the attack then disappears, the general nutrition not being markedly impaired; in the severe form the inanition may be so great that the disease may become extremely serious, or even fatal.

*Juvenile Vomiting.*—This form of vomiting occurs in young school children who have been subjected to overstudy. In addition to the vomiting, other symptoms, as a rule, present themselves. The disorder usually begins with gastric pains and vomiting, to which such symptoms as headache, pallor, dilated pupils, a slowing of the pulse, and constipation are added. In these cases improvement always follows when the patient is allowed to discontinue his school work.

*Periodic Vomiting in Children.*—A peculiar form of periodic vomiting, differing from the form described as juvenile vomiting, occurs in young children. It comes on usually at the age of from two to three years, and generally passes off as the child becomes a few years older. The condition has been fully described by Snow, Griffith, and others. The attack is characterized by a sudden onset, in the midst of good health, of intense vomiting, accompanied by fever and great depression, that ceases as suddenly as it began. In a certain number of cases the attacks appear with a distinct periodicity at intervals of every few weeks or even months. In at least some Snow has shown that the gastric irritability is due to an intermittent hyperchlorhydria, a secretory gastric neurosis. The cause of this recurrent vomiting is unknown, but it is probably a transitory auto-intoxication that affects the nerve centres governing gastric secretion and motion.

3. **Reflex Vomiting.**—This is a very common form of nervous vomiting, and may be produced by various diseases affecting the stomach and other organs. It is found as one of the symptoms of disease of the middle ear, disturbances of the eye, pharynx, larynx and tonsils. To these may be added diseases of the lungs and abdominal organs. Reflex vomiting is also common during pregnancy.

Gould and others have pointed out the frequent dependence of this as well as other gastric neuroses upon eye-strain, while Brav has found astigmatism a common cause of vomiting in school children. The vomiting of pregnancy is often a reflex neurosis of the sympathetic nerves. In another form vomiting is due to some hysterical or neurasthenic tendency. In these cases the neurotic nature is indicated by the fact that a cure frequently follows the employment of perfectly useless and unphysiological procedures. Many of these cases, therefore, may be cured by rest or simple suggestive means. A third variety of vomiting of pregnancy is the toxemic form, which is a very serious disease and is produced by a marked disturbance of metabolism.

**Diagnosis.**—The diagnosis between the various forms of nervous vomiting is not always a simple matter. After establishing the nervous origin of the vomiting it is most important to determine its exact cause, whether, for example, it is reflex or due purely to neurasthenia. These facts, as a rule, can be elicited by a complete investigation into the history and a rigid examination of the patient.

**Prognosis.**—This depends largely upon the cause. In the cerebro-spinal vomiting it is usually bad, although in the gastric crises the vomiting may abate entirely, notwithstanding the continued progress of the disease. In the form with neurasthenia or hysteria the prognosis is usually favorable when under proper treatment, but occasionally a

fatal outcome is met with, due to exhaustion occasioned by the continued and prolonged vomiting. Three cases of this character have come under the observation of the writer. In the reflex form the prognosis is favorable provided the cause can be removed.

**Treatment.**—The chief aim is removal of the cause. Inasmuch as this is not always possible, many patients must be treated symptomatically. In the milder forms, change of scene, avoidance of mental excitement, and rest will overcome this condition. In severe cases patients should always be placed in bed in a hospital under rigid isolation and rest-cure treatment. In seven of this series the writer is convinced that the lives of the patients were saved by this plan of treatment.

As regards diet, the patient should be fed on liquid food, given in very small quantities, such as champagne, ice-cold milk, clam broth, or cold egg-albumen. In severe forms the patient must be fed for some days exclusively by the rectum and the thirst relieved by saline enemata. Duodenal alimentation by means of Einhorn's duodenal tube has proved highly efficacious in a number of cases under the writer's care. In some cases solid foods are well borne when liquids cannot be taken. These should be given in very small quantities; scraped beef, eggs, rice, and toast are especially useful. Hydrotherapy may be practised with good results in some cases. Electricity has a beneficial effect in some instances, the galvanic current being used with the anode in the stomach and the cathode on the spinal column. The writer has had good results at times from lavage with solutions of nitrate of silver, at other times with solutions of menthol. As to the drugs used with more or less effect the following may be mentioned: Morphine given hypodermically, oxalate of cerium, cocain, menthol, the bromides, chloral, validol, and orthoform. Boas recommends iodide of potassium and bromide of sodium in the gastric crises, and rectal suppositories of opium and belladonna are useful in attacks of periodic vomiting. In the periodic vomiting of children Rachford suggests the use of calomel and bicarbonate of soda, followed by a saline laxative, and then benzoate of soda in from 3 to 8 grain (0.2 to 0.5 gm.) doses every two or three hours. Snow also recommends an alkaline treatment in these cases.

### NAUSEA NERVOSA

Nausea is observed in many gastric affections, as well as in diseases of other organs. There is, however, a purely functional form of nausea which is entirely of nervous origin and is due to hysteria or neurasthenia.

**Etiology.**—Nausea nervosa is often found in anemic and chlorotic females; it is also observed with menstrual disturbances and frequently at the menopause. It begins, as a rule, after great excitement, worry, or anxiety in neurasthenic or hysterical individuals. This disorder is most often observed in women and rarely in men. In the series of 1592 cases of gastric neuroses there were 40 cases of nausea nervosa (2.5 per cent.), 30 in females and 10 in males. As to age, 13 were in the second decade, 9 in the third, 7 in the fourth, 7 in the fifth, and 1 in the sixth.



**Symptoms.**—Nausea may be intermittent or continuous. In the intermittent form it appears any time of the day or night and bears no relation to the ingestion of food, its quantity or quality. In the continuous form it persists for days and months in varying degrees of severity, sometimes slight, at other times so intense as to cause vomiting. The nausea is not dependent upon the quantity or quality of the food ingested, yet it causes a loss of appetite, and the patients, as a rule, live upon a very limited diet, the result being great emaciation. Examination of the gastric contents showed a normal acidity in 34 and in 6 a hyperacidity. The gastric motility was normal in all.

**Diagnosis.**—All organic diseases accompanied by nausea must be excluded, such as tuberculosis, diseases of the genital organs, arteriosclerosis, uremia, and organic diseases of the stomach.

**Treatment.**—In many cases due to anemia or chlorosis appropriate treatment will relieve the condition. Attention should be paid to repair of the nervous system, especially by massage, electricity, and hydrotherapy. In those cases accompanied by marked anemia and great loss of flesh splendid results are obtained through a well-conducted rest cure. Complete isolation is always necessary in severe forms. Duodenal feeding may be practised at times with advantage. Relief is shown in some cases by means of the bromides, valerian, sumbul, and chloral. Validol for milder forms has been of great service in the writer's experience.

### CARDIOSPASM

Cardiospasm is characterized by a spasmodic contraction of the cardia not due to any organic disease. Under normal conditions there is a spasmodic contraction of the cardia by which not only solids but also liquids are somewhat delayed in their passage into the stomach. This contraction may be increased both when the cardia is the seat of an organic disease or as a condition accompanying hysteria or neurasthenia. As a result of the cardiospasm a diffuse dilatation of the œsophagus is often produced. The etiology of cardiospasm and diffuse dilatation of the œsophagus has been a matter of dispute. According to Mikulicz and Meltzer, it is due to a failure of the central inhibitory influences controlling contraction of the cardia. Rosenheim believes that the predisposition to idiopathic dilatation is due to a weakness of the muscular coats; while Krause views it as a functional disturbance of the innervation of the œsophagus causing cardiospasm as well as a weakness of the muscular wall (Tyson).

**Etiology.**—Cardiospasm is found at times accompanying hysteria and neurasthenia. It occurs after swallowing food that is hard and not sufficiently masticated, or after swallowing food too rapidly or too highly seasoned. Excitement is occasionally a causative factor. It occurs at times after habitual air swallowing. If the air collects, it expands and produces a dilatation of the stomach, and with it a spasm of the cardia, often complicated at the same time with pylorospasm. It occurs at any age, most frequently in females. In this series of 1592 cases of gastric neuroses there were 25 cases of cardiospasm (1.5 per cent.), 17

being females and 8 males. As to age, 6 were in the second decade, 9 in the third, 7 in the fourth, 2 in the fifth, and 1 in the sixth.

**Symptoms.**—Cardiospasm occurs in two forms, as the acute or chronic variety. The acute form is only of a few days' duration, the onset being sudden. The attack is accompanied by a burning sensation, with pressure or pain behind the sternum, and dysphagia; as the food accumulates in the œsophagus an effort must be made to force it into the stomach; when this is impossible, the food is regurgitated, causing at times some dyspnoea. At other times it is impossible to swallow food. Regurgitation of the food causes relief of all symptoms. This condition comes on periodically, and during the interval the patient is free from discomfort. In the chronic form there is also a marked dysphagia. Foods are forced into the stomach by the patient with great effort, by taking a deep inspiration and compressing the chest by muscular action while holding the breath. Liquids and semisolids are most easily swallowed. The solid foods must be thoroughly masticated, and are often swallowed by taking small quantities of water at the same time. After a time a diffuse dilatation of the œsophagus takes place, which may hold several hundred cubic centimeters. At times less difficulty occurs in swallowing, and occasionally the patient can take a solid meal; however, after the diffuse dilatation of the œsophagus has taken place, the dysphagia becomes constant. If the air swallowed during a meal cannot be eructated, the stomach becomes distended, and on account of the cardiospasm it is impossible for vomiting to take place. Pain and pressure behind the sternum are common, the patient complaining of a sensation as though food were lodged at this point. The dilated lower part of the œsophagus retains the food and regurgitates it after a certain length of time. The contents contain no free hydrochloric acid. The second deglutition murmur is absent. Examination with the bougie reveals important conditions; on introducing it one feels a resistance, which is felt more plainly with the large than with the small-sized bougies; after gentle pressure the resistance gives way and the bougie passes into the stomach. The presence of a diffuse dilatation of the œsophagus above the position of the cardiospasm is demonstrated as follows: A tube is passed in the œsophagus to a point at which food mixed with mucus is withdrawn through the tube. A second tube is now passed into the œsophagus beside the first, but is forced through the resistance; through this tube gastric contents are obtained; if eosin-stained water is introduced through the first tube and plain water through the second, it can be demonstrated that there is no communication between the tubes, as is observed by the return of the fluids separately and not mixed (Rumpel's double tube test). Owing to the lack of nourishment, the general health fails.

**Diagnosis.**—In the acute form this is made by the variations in the degree of dysphagia, by the introduction of an œsophageal bougie without difficulty, by the resistance being less from a bougie of large caliber than from a small one, by the absence of the second deglutition murmur, and by the inability of the patient to vomit. In the chronic form the dysphagia lasts over a longer period of time, while symptoms of dilatation of the œsophagus become evident. The condition is recognized by the

test of Rumpel, already described. In addition, the examination by means of the bougie reveals a condition similar to that found in the acute form. In those cases accompanied by dilatation the diagnosis may be confirmed by means of œsophagoscopy and an x-ray examination. Cardiac carcinoma is differentiated by the fact that it occurs in advanced age, that often traces of blood and pus, together with carcinomatous particles, are obtained by the bougie, and that small-calibered bougies pass more easily than larger ones. In cardiac cancer there is usually an absence of free hydrochloric acid in the gastric secretion, while in cardiospasm there is either a normal or a hyperacid secretion.

**Treatment.**—In the acute forms special attention should be paid to the nervous system and the general nutrition of the patient looked into. In order to overcome the cardiospasm large bougies should be introduced into the stomach and allowed to remain for a considerable length of time. Internally belladonna, the bromides, morphine, and cocaine are used with a variable degree of success. Rosenheim recommends the injection at the seat of the affection of a 3 to 5 per cent. eucaïne solution, at first twice daily, then less frequently. In the treatment of the chronic form only liquid or semisolid food should be taken; in those cases in which the constriction is marked food must be administered through a tube; before proceeding with the feeding, lavage of the œsophagus is first practised with the same tube, in order to rid it of mucous masses, food remains, etc. Large bougies should also be introduced and allowed to remain for a considerable length of time. In order to produce a forcible dilatation of the contracted œsophagus and cardia, Sippey's, Plummer's, Einhorn's or Meyer's dilators are employed with much success.

### PYLOROSPASM

By pylorospasm is meant a spasmodic contraction of the pylorus not due to organic disease. It is usually due to some severe irritation of the mucosa of the pylorus, such as that produced by the acid in superacidity or supersecretion; or it may be due to an ulcer, erosions, fissures, or cancer at the pylorus, while there are other forms entirely of nervous origin. Cases of the latter form have been described in infants. In a female, aged twenty-three years, observed by the writer, in whom all the symptoms of pylorospasm were manifested and who was operated on by Finney, no anatomical changes were observed, but entire relief was afforded by pyloroplasty.

**Etiology.**—In the series of gastric neuroses only 4 cases could be definitely classified as primary pylorospasm (0.3 per cent.); 3 of these were observed in females and 1 in a male.

**Symptoms.**—At the height of digestion, the pylorus suddenly becomes spasmodically contracted with intense pain in its region, together with eructations and often vomiting. At first the spasm appears periodically, but as the disorder progresses it may become continuous and produce a spastic contraction of the pylorus, with tendency to dilatation and retention of food. The food is vomited under these conditions, and possesses all the characteristics of that observed in a dilated stomach.



Relief is afforded by the vomiting for a period of time varying from one to three or four days, when the same disturbance is again produced. The symptoms found in dilatation are then observed—emaciation, intense thirst, and constipation. The pyloric area, as a rule, is tender to pressure, and contraction may take place near the pylorus, producing a firm mass on palpation, which may gradually disappear. The secretion of acid may be normal or increased, but becomes normal when the motor function is again restored. Chronic gastrosuccorrhœa is frequently observed in these cases and occasionally tetany.

**Diagnosis.**—This is made by the exclusion of all organic disease and the appearance of the spasmodic attacks of pain in the region of the pylorus, with the appearance of intermittent stagnation.

**Treatment.**—This consists primarily in properly looking after the underlying neurasthenia. For this purpose change of scene, massage and electricity, or a rest cure, may be found advisable. The diet should be carefully regulated, all irritating foods being avoided, and the meals should be small, easily digested, and given at regular intervals. The administration of olive oil has been found of great service. When retention is present, gastric lavage with plain water or nitrate of silver solution must be given. For the pain codeine combined with belladonna is serviceable; hot applications to the abdomen and a thorough lavage usually afford most relief from the pain. Einhorn has recommended the dilatation of the pylorus by means of his pyloric dilator. If after faithful trial no relief can be obtained from these measures described, the writer has observed excellent results from pyloroplasty. Some authorities recommend gastro-enterostomy.

## PNEUMATOSIS

By pneumatosis is meant that condition in which the stomach is distended with air and in which expulsion of the same is impossible, causing unpleasant expansion of the stomach and dyspnœa (asthma dyspepticum, Henoeh). In a large proportion of cases this condition is partly due to a simultaneous cardiospasm and pylorospasm. Relief is at once afforded when the spasm ceases and the air escapes. Pneumatosis is found secondary to certain gastric disturbances, such as atony and dilatation, or is a primary neurosis accompanying neurasthenia and hysteria. It occurs as a continuous or periodic affection, and appears after nervous anxieties or mental strains.

**Etiology.**—Pneumatosis is found more often in males. In this series it occurred in 8 cases (0.5 per cent.); of these, 6 were males and 2 females.

**Symptoms.**—Pneumatosis occurs in one of two types: In the first it appears in an acute form intermittently with alarming symptoms causing dyspnœa, collapse, rapid and irregular pulse, and cyanosis. The region of the stomach is greatly distended, often balloon-shaped, and is tympanitic on percussion. The patient is unable to relieve himself by eructating. In the second type the attacks either come on immediately after meals or some time later, or after some exertion; the symptoms are much like

those of the acute form, but may become alarming. The gastric contents are usually normal; occasionally there is a hyperchlorhydria, and again at times hypochlorhydria.

**Diagnosis.**—This is ordinarily made by observing the symptoms described; all organic conditions such as dilatation or atony must be excluded. It is sometimes mistaken for angina pectoris, but in angina there is no continuous distension of the stomach and the expulsion of the gas does not afford relief.

**Treatment.**—Special attention should be paid to the nervous system. Change of scene, hydrotherapy, and massage will often do much to restore the patient to health. Of the medicines used to give relief the most important are the bromides, cocaine, or morphine. Boas advises the use of the extract of physostigmine, grain  $\frac{1}{6}$  (gm. 0.01), combined with the extract of nux vomica, grain  $\frac{1}{3}$  (gr. 0.02), three times daily. In acute attacks the stomach tube will afford instant relief.

### PERISTALTIC UNREST (TORMINA VENTRICULI NERVOSA)

Peristaltic unrest is characterized by an excessive and visible peristalsis of the stomach. This condition was first described by Kussmaul as occurring in neurasthenic individuals in whom excessive peristalsis caused annoying sensation and unpleasant contractions of the stomach. In the cases described by Kussmaul the peristaltic movements were visible, as a gastropsois was present at the same time. Peristaltic movements usually take their origin at the fundus of the stomach and run toward the pylorus; the wave, however, may be antiperistaltic also and run in the opposite direction; occasionally antiperistaltic movements exist alone; cases have also been observed in which peristaltic movements of the intestines were present at the same time.

**Etiology.**—Peristaltic unrest may occur in one of two conditions: First, due to an obstruction of the pylorus, the stomach exerting itself to overcome the difficulty produced in emptying its contents into the intestines; second, the unrest may occur as a pure neurosis, accompanying neurasthenia or hysteria; as a neurosis it is an exceedingly rare affection, but one case occurring in the series (0.06 per cent.).

**Symptoms.**—The important symptom is the peristaltic movement of the stomach running from the fundus to the pylorus and at times accompanied by antiperistaltic movements. These movements are usually visible and are felt by the patient. When the stomach is in its normal position the patient may be conscious of the movement, but it cannot be seen. Other symptoms are often present, such as eructations, nausea, anorexia, and the too rapid evacuation of the stomach (hypermotility). General symptoms of neurasthenia are ordinarily present.

**Diagnosis.**—This is simple if organic obstruction of the pylorus can be excluded, which is usually readily done.

**Treatment.**—This should be directed mainly toward the neurasthenic condition by change of scene, massage, and hydrotherapy. At times, when the patient is anemic, the best results have followed a well-regulated

rest cure. Kussmaul recommends internal and external application of the faradic current. Good results have been obtained by the administration of the bromides, codeine, and belladonna.

### SUBACIDITY OR HYPOCHLORHYDRIA

By subacidity or hypochlorhydria is meant that form of neurosis in which the amount of hydrochloric acid as well as the other constituents of the gastric secretion is lessened. While there are still small quantities of hydrochloric acid secreted in this condition, the quantity is so small that it at once combines with the protein foods. Subacidity is present in certain organic diseases of the stomach, as chronic gastritis and cancer, also during the height of acute febrile diseases. The term nervous subacidity, however, can only be applied to those conditions in which all signs of organic disease of the stomach can be excluded. The condition is frequently found accompanying neurasthenia or hysteria, and is present also in certain lesions of the spinal cord, as *tabes dorsalis*. In this series of 1592 cases, 80 (5 per cent.) represent the number of cases of subacidity or hypochlorhydria; of these, 34 were males and 46 females.

**Symptoms.**—Many cases run their course for a considerable period of time without symptoms; this is especially true as long as the motor function of the stomach is normal, but as soon as this is impaired fermentation begins in the intestines and distension from gas takes place. The symptoms of this condition, however, are not distinctive, and a diagnosis cannot be made until the gastric secretion is examined. As long as the intestinal digestion is normal, symptoms of gastric disturbances are absent and the patient can maintain his normal weight and strength; as soon, however, as the intestinal functions become disordered by inflammation, diarrhoea sets in and the patient becomes weakened and emaciated. A symptom in 7 cases was burning with pain about two hours after meals, relieved by alkalis or food and presenting symptoms of acidity.

**Diagnosis.**—This is arrived at by examination of the gastric contents and finding a diminution of hydrochloric acid; at the same time hysterical or neurasthenic symptoms must be present. By continually observing cases of nervous subacidity one is frequently surprised by the various changes this condition undergoes, often to a normal acidity or even to hyperacidity. Hemmeter termed this condition *heterochylia*.

**Treatment.**—The diet should consist largely of carbohydrates. Meat should be given, however, in the most digestible form and finely divided; the food should be given in small quantities at frequent intervals. Much attention should be paid to the general health and special treatment should be given to the nervous system. Hydrochloric acid administered in 10- to 20-drop (1 cc.) doses after meals is a useful adjuvant. Lavage of the stomach is rarely necessary unless the motor function is markedly disturbed and at the same time leads to fermentation. The use of massage and electricity (intra-gastric) is also serviceable in many cases. The saline waters, such as Kissingen or Wiesbaden, are useful so long as the motor function is normal; as soon as this is disturbed their use should be discontinued.



## ANACIDITY OR ACHYLIA GASTRICA

The term achylia gastrica was first introduced by Einhorn<sup>1</sup> to indicate a condition in which there is an absence of gastric secretion. The term is simply meant to designate a symptom, the condition underlying the same being a severe form of chronic gastritis or atrophy of the mucous membrane or some condition wholly neurotic in origin. It is not our province to discuss here the cases which are accompanied by a complete atrophy of the gastric mucous membrane. Fenwick<sup>2</sup> first described this condition in certain cases of pernicious anemia. The use of the term achylia gastrica is best restricted to those cases for which Einhorn first adopted it. In these there is a complete lack of gastric secretion, which persists for many years without ending fatally, and in which the general condition of health frequently improves. The patient often presents no subjective symptoms whatever, and can take many forms of food without the slightest discomfort, the small intestine vicariously assuming the function of the stomach. In a case of the writer's this condition persisted for twelve years, with gain in weight and with but few attacks of intestinal disturbance.

**Etiology.**—It seems doubtful in most instances whether a complete absence of gastric secretion is due to a neurasthenic condition alone, because, while the neurasthenic condition may improve and disappear, the gastric secretion remains absent permanently. According to many writers it is probable that a more or less pronounced chronic gastritis is present in a large proportion of cases of achylia gastrica. According to Martius, achylia gastrica is produced by two conditions: First, simple achylia gastrica, a primary secretory debility of the stomach that may be either congenital or developed early from hereditary predisposition; and second, atrophy of the gastric mucosa producing a secondary achylia gastrica. Simple achylia gastrica is found in neurasthenic patients, and is associated with inherited weakness of the nervous system. It may remain latent without making serious inroads upon the general health, especially in those patients in whom the motility of the stomach remains normal and the intestinal functions are undisturbed. There are transitions from the simple forms of achylia gastrica in which there are none or but the slightest changes in the mucous membrane to that form ending in complete gastric atrophy.

According to Stockton, the belief that achylia gastrica may in some instances begin as a simple depression of the functional activity of the secretory glands of the stomach, the result in some cases of neurasthenia, in others as reflex irritation, appears to be gaining rather than losing ground. According to this observer, with the improvement in health gastric secretion is increased, and disappears again with nervous strain. When it is absent for any length of time, it is probable that considerable atrophy of the mucous membrane has appeared, and yet in certain cases Stockton observed the secretion appearing after it had been absent for a period of a year or more. From an observation of some patients for

<sup>1</sup> *New York Med. Rec.*, June 11, 1892.

<sup>2</sup> *Lancet*, July, 1877.

at least fifteen years, Stockton<sup>1</sup> believes that, in the absence of or with a very low standard of gastric secretion, individuals are always found to have impaired health, even with relatively good intestinal digestion.

Achylia gastrica is usually found after the thirtieth year of age; it is rarely found in younger persons. There is apparently no difference in the frequency of occurrence in males or females. In this series the number of cases of achylia gastrica is 114; of these, 2 represent that form known as atrophy of the stomach, and cannot be considered here, leaving 112 cases (7 per cent.) in all, 57 being females and 55 males. As to age, 2 were below twenty, 13 in the third decade, 19 in the fourth, 33 in the fifth, 35 in the sixth, and 10 in the seventh.

**Pathology.**—There have been so few cases in which autopsies have been performed that it is not known whether lesions occur in all cases. According to Martius and Lubarsch, and Strauss,<sup>2</sup> a more or less marked gastritis exists in a large proportion of cases of achylia, but there is no means of determining whether the gastritis is the cause or the result of the achylia. Einhorn maintains that there are many cases of achylia in which the mucous membrane of the stomach presents no pathological change whatever, which accounts for the fact that a repair of the condition is sometimes found. Small fragments of the mucous membrane that are broken off by the stomach tube usually present some degenerative change. The glands show granular degeneration with considerable round-cell infiltration presenting the picture of a glandular gastritis. It is generally believed by most authorities that notwithstanding the impossibility of judging the general condition of the mucous membrane from fragments of a small area, in the largest proportion of cases of achylia gastrica there is some degeneration in the mucous membrane of the stomach, and there is no great amount of evidence at present to indicate that this condition can occur without some anatomical change.

**Symptoms.**—Einhorn<sup>3</sup> divides achylia gastrica into three groups: (1) In individuals having no gastro-intestinal symptoms whatever, and who are in good general health. (2) Patients presenting a greater or less number of gastric symptoms. (3) Patients having apparently no gastric symptoms, but presenting marked intestinal disturbances. The smallest number of cases are contained in the first group, in which all subjective symptoms are absent. The individual presents no loss of weight, the appetite remains unimpaired, and the diseased condition is usually noted by accident. In this series of 112 cases, only 8 can be counted in this group.

The largest proportion of cases is found in the second group, in which the symptoms are mainly gastric; in this series of 112 cases, 69 belong to this group. The symptoms are loss of appetite, sensations of pain and pressure in the region of the stomach, and occasionally vomiting. The pains are generally mild, often merely a sensation of burning and pressure occurring soon after meals and persisting for some time; in some cases there may be no pain whatever, while in others it may occur

<sup>1</sup> *New York Medical Journal*, February 17, 1906.

<sup>2</sup> *Virchows Archiv*, Bd. cliv.

<sup>3</sup> *Diseases of the Stomach*, fifth edition, p. 352.

with great severity. Nausea and vomiting occur rarely—in but 17 cases of this series. The vomited matter usually contains undigested food particles. Eructations and pyrosis are observed at times; occasionally symptoms are presented which are similar to those found in hyperchlorhydria; that is, the appearance of pain one or two hours after meals, relieved by the ingestion of food. This symptom was noted in 11 cases in this series. Nervous symptoms are also frequently present.

The third group contains those patients having apparently no gastric disturbance but presenting intestinal disturbances. In the series of 112 cases these number 35. The most prominent symptom is diarrhœa. The patient complains of little or no disturbance of the stomach, but is affected with symptoms apparently referable to marked disturbance of the intestines, gurgling in the bowels and intestinal colic. Frequently diarrhœa alternates with constipation. The diarrhœa is probably occasioned by the undigested food mechanically stimulating peristalsis. In addition, a large number of bacteria pass through the stomach and cause decomposition in the bowels.

Examination of the gastric contents is of the greatest importance. The following are the characteristics: the amount is very small, only a small quantity of fluid, with bits of unaltered bread; in the morning before the ingestion of food the stomach is entirely empty, with no traces of food from the previous day. The gastric contents are neutral or slightly acid, the total acidity varying between 2 and 6. Hydrochloric acid is not present, pepsin and rennin are entirely absent, although the rennet zymogen may still be present; the test for propeptones and peptone reveals negative results, and there is an absence of mucus. Fragments of mucous membrane often appear in the contents, indicating the great vulnerability of the mucous membrane. The motor function of the stomach is usually increased.

**Diagnosis.**—For the most part this is not difficult from the examination of the gastric contents; repeated examinations are necessary to confirm it. The most important signs are an entire and constant absence of hydrochloric acid, an almost entire absence of the ferments, and a very low total acidity. As in nearly all of the cases some alteration has taken place in the gastric mucosa, it is difficult in many instances to distinguish this condition from a chronic gastritis. One must rely mainly upon the presence of nervous symptoms and the complete absence of mucus; a fluctuation in the gastric secretion will occasionally indicate the nervous origin. This condition is distinguished from carcinoma by the absence of the typical signs of cancer. The degree of acidity is much higher in carcinoma even when free hydrochloric acid is absent; lactic acid is usually present as well as the Oppler-Boas bacillus; the latter is not found in achylia. There is a constant finding of occult blood in carcinoma never observed in achylia; in 50 examinations from 24 cases of achylia in this series, occult blood was never found in the feces. Hemorrhages are never observed in achylia. When cancer is advanced, no difficulty is presented in making the diagnosis.

**Course and Prognosis.**—Patients suffering from achylia gastrica may be affected for many years without having serious inroads made in their



general health. They may even gain flesh when the course is latent for a long period of time. As long as the motor functions of the stomach remain normal and the intestine takes up the functions of the stomach vicariously, no serious results are produced; when, however, one or other of the functions are disturbed, the symptoms of achylia begin to manifest themselves and the general nutrition becomes markedly disturbed. Since a chronic gastritis is present in most instances, an absolute cure is impossible, even though the symptoms are entirely relieved.

**Treatment.**—This is mainly dietetic, and although it is necessary to restrict the diet materially, it is most important to insist on the ingestion of sufficient food, as many of these patients are weak and have lost flesh. The question as to quantity of food should be carefully considered with an attempt to increase the general nutrition as well as the body weight. In accomplishing this object these facts should be held in mind, namely, to maintain the motor function of the stomach in its normal condition, as well as to prevent any disturbance of the intestinal canal, since the intestine acts vicariously and digests the food for the stomach. It is important to arrange the diet so that it can be acted upon easily by the intestinal juices. The food must be broken up into as fine particles as possible and should to a large extent be given in liquid and semiliquid form. Of the liquids, broths, such as barley, rice, or chicken, are to be recommended. Vegetables are usually well taken; cereals should be eaten after the cellulose has been removed. Peas and beans strained and eaten in purée form, as in broth, are especially useful, since they contain quite a large percentage of protein. Potatoes and rice should be eaten cooked with broth or milk, or as a mush. Eggs are best taken soft boiled. Meats must be given in the most digestible forms, *i. e.*, brains, scraped beef, boiled sweetbreads, and these only in small amount; raw oysters and boiled fish are also permissible. Milk is occasionally imperfectly digested and cream, kefir, koumyss, or matzoon may be substituted. Butter may be eaten on crackers, stale bread, or toast. Such beverages as tea, coffee, cocoa, and small quantities of wine may be allowed. When symptoms of hyperchlorhydria are manifested, the taking of liquids from one to two hours after meals will afford relief.

Lavage and intragastric faradization may be resorted to in those instances in which the gastric motility is somewhat impaired. Drugs are not always required; in some cases dilute hydrochloric acid may be given, well diluted in 15-drop (1 cc.) doses, three or four times at intervals of fifteen minutes after meals with benefit. For anorexia strychnine combined with the bitter tonics is recommended. In those instances in which the general nutrition has become very much depressed, and in which diarrhoea is or is not present, excellent results may be obtained by a systemic rest-cure treatment.

### ACORIA

By acoria is meant that condition in which there is an absence of the sensation of satiety. The patient does not feel that he has eaten enough, no matter whether he partakes of a large or a small meal; the

appetite is not increased; it may even be diminished. The cause has not been determined; it has been stated that acoria is due to an overstimulation of the hunger centre, but this theory is untenable. The condition may be due to loss of sensation in the stomach itself.

**Etiology.**—Acoria occurs as a primary disorder associated with neurasthenia or hysteria, or is observed secondary to other diseases, such as diabetes or disorders of the male sexual organs. Sorrow, sudden shock, or excitement are among the etiological factors concerned in its production. In this series of 1592 cases it occurred five times (0.3 per cent.); of the 5 cases, 3 occurred in males and 2 in females.

**Symptoms.**—The affection is characterized by an absence of the sensation of satiation, no matter how large the meal may be. In consequence of the inordinate eating, atony and gastritis may develop. Acoria may at times be transformed into bulimia. The gastric secretion is usually normal; in this series normal acidity existed in 4 and subacidity in 1; the gastric motility was normal.

**Diagnosis.**—Acoria must be differentiated from polyphagia and bulimia; in acoria there is an entire absence of the sensation of satiation, while in polyphagia the feeling of satisfaction is delayed to such an extent as to create a constant desire for more food. In bulimia there is an abnormal desire for food, but this desire can be satisfied.

**Treatment.**—This must be directed toward the cause, which in most instances involves treatment of the general neurasthenia by means of rest, change of scene, hydrotherapy, massage, and electricity. Entire relief was effected in two cases by a rest cure combined with psychotherapy. The meals should be carefully regulated; the patient should be required to eat slowly and masticate thoroughly. Strychnine in ascending doses has been used with some success.

### ANOREXIA NERVOSA

Anorexia is characterized by a marked diminution in or the absence of the sensation of hunger, combined with a complete loss of appetite. Penzoldt points out that the terms hunger and appetite should be separated, as they are not synonymous; according to this author, hunger is defined as the warning for food, while appetite is the pleasure in partaking of it. Anorexia may accompany various organic or functional diseases, or may be a primary neurosis accompanying neurasthenia or hysteria (anorexia nervosa). In this condition the loss of appetite may be so great as to cause a most marked disgust or repugnance for food. The cause of nervous anorexia has been attributed to a depressed state of the hunger centre, while it is generally believed that this affection is produced by a "special hyperesthesia" of the mucous membrane of the stomach (Rosenthal).

**Etiology.**—Anorexia may be primary or secondary. It is primary as a manifestation of hysteria and neurasthenia; it is secondary to such diseases as cancer of the stomach, chronic gastritis, gastroptosis, acute febrile conditions, chronic nephritis, and other organic diseases. Anorexia nervosa usually begins after some great mental strain, excitement, or

anxiety. It is not uncommonly found in men with sexual disorders (Peyer) and in women affected with uterine disease, and is often observed in a most aggravated degree in the insane (anorexia mentale). Opium habitués are commonly affected with this disorder. It is most frequently observed in females, and especially between the ages of fifteen and forty years. In this series of 1592 cases there were 48 cases of nervous anorexia (3 per cent.), 11 being males and 37 females. As to age, 19 were in the second decade, 12 in the third, 10 in the fourth, 4 in the fifth, and 3 in the sixth.

**Symptoms.**—After some great mental strain or worry a loss of appetite begins to manifest itself; the digestive powers are still normal but the patient shows a lack of desire for food. This lack of appetite becomes more and more decided until the stage of absolute repugnance for food is reached, and the patient loses weight and strength, becomes anemic and pale, the pulse becomes slow and weak, the urine scanty, and marked constipation is evident. With these symptoms, others of a nervous character manifest themselves, and the patient becomes irritable, restless, and sleepless, and, if forced to take food, vomits. If the condition still progresses, symptoms of a very serious character arise, such as inanition with delirium, slight fever, and exhaustion, and the patient may die. When the disease is well marked the patient presents the appearance of having tuberculosis; the skin is dry, the abdomen is markedly retracted, the eyes are sunken, the pupils are dilated, and the mucous membranes are pale. Death may be due to exhaustion, pneumonia, or infection.

**Diagnosis.**—The presence of other nervous manifestations, together with the anorexia and absence of all organic disease, easily leads to a correct diagnosis. In all cases, in arriving at a diagnosis organic diseases accompanied by anorexia must be excluded.

**Treatment.**—In the milder forms much can be accomplished by insisting that the patient take sufficient nourishment. In order to make this possible the food should be varied and the patient's taste so far as possible be consulted. The bitter tonics at times play an important rôle; of these, gentian, colomaba, quinine, and strychnine are often useful, especially when combined with dilute hydrochloric acid. Lavage with a bitter infusion, or with a 0.5 per cent. solution of sodium chloride, has been recommended by Kussmaul and Fleiner. The nervous system should be built up by means of massage, hydrotherapy, and electricity. In all serious forms the patient should be isolated in a hospital or sanitarium and placed under a strict rest cure, with forced feeding. The writer feels confident that the lives of a large number of his patients were saved by insisting upon this method of treatment. In those instances in which the patient still refuses to take food, gavage should be practised. When improving, some form of iron is useful.

### SITOPHOBIA

This term was first introduced by Einhorn to indicate a special neurosis of the stomach manifested by marked fear of food. He declared that if this condition continued the dyspeptic symptoms gradually



increased, even after taking the smallest quantities of food. In consequence the patient loses much flesh, becomes anemic, and develops other neurasthenic symptoms, such as dizziness, headaches, lassitude, etc. The fear is due to the unpleasant sensation and pain which occur after eating, in consequence of which the patient gives up one form of food after another until extremely small quantities of nourishment are taken and signs of inanition are produced.

**Etiology.**—Sitophobia may exist secondarily to organic or functional disorders of the gastro-intestinal tract, or be a neurosis due to hysteria or neurasthenia. As a secondary condition it is found in ulcer, chronic gastritis, cancer of the stomach, chronic constipation, chronic diarrhœa, gastralgia, and enteralgia. In the series of 1592 cases of gastric neuroses there were 24 cases of sitophobia (1.5 per cent.), 18 being females and 6 males. As to age, 4 were in the second decade, 7 in the third, 3 in the fourth, 6 in the fifth, 3 in the sixth, and 1 in the seventh.

**Symptoms.**—On account of pain or uncomfortable sensations in the stomach the patient gives up one food after another until he subsists on a very small quantity of liquid food; in consequence of which the symptoms of inanition are produced. These are indicated by severe headaches, nervous manifestations (vertigo, general aches and pains), great loss of strength and flesh, and marked anemia. Many of these patients consume only from 400 to 1000 calories per day; if this persists, the emaciation continues until the patient finally succumbs.

**Treatment.**—It is necessary to insist that the patient make every effort to take nourishment, even though it produces pain. In following out this plan he will observe that food which at first occasioned uncomfortable sensations gradually loses this effect and can be taken without fear of distress. At first liquid food alone should be given in the form of milk or egg-albumen, and gradually the diet should be increased to the soft and then to the solid form. In severe cases marked results are obtained by a well-regulated rest cure. It is an excellent plan to persist with liquid food, such as milk and eggs, for from ten to twelve days of the rest treatment, then increasing to very large quantities, and later suddenly placing the patient upon a generous diet without attracting his attention to the same. The patient gradually gains much in weight and strength by this plan of treatment. Occasionally the bromides, belladonna, and hyoscyamus are useful in reducing the sensitiveness of the stomach.

### INCONTINENCE OF THE PYLORUS

Attention was first called to insufficiency or incontinence of the pylorus by de Sère and later by Epstein. The pylorus is insufficient when, during digestion, it is incontinent and fails to prevent the chyme from proceeding into the intestines at a too rapid rate.

**Etiology.**—The condition may be due to an organic disorder, or may exist as a neurosis. The organic conditions that may produce the insufficiency are carcinoma or ulcer of the pylorus or chronic gastritis. Boas has observed it in duodenal stenosis in which the pylorus was dilated by the material accumulating above the stenotic area. As a neurosis,

incontinence of the pylorus is a very rare affection. In the series studied there were but two cases (0.1 per cent.), one in a male aged twenty-seven years, the other in a female aged forty-one years.

**Symptoms.**—This condition becomes evident by the fact that on inflation of the stomach this organ does not become filled and distended, but instead a gurgling takes place at the pylorus, the escape of air causing increased intestinal tympany. In addition, the stomach empties itself too rapidly after test meals and other meals, and there is a reflux of considerable quantities of intestinal contents, bile, and pancreatic secretion into the stomach. This is observed in almost every lavage. Because of the very rapid evacuation of the stomach, diarrhoea is common.

**Treatment.**—Because of the passage of the undigested food into the intestines and the diarrhoea, food should be given in a very digestible form. Einhorn recommends direct gastric faradization and occasional lavage. In some instances strychnine has been of service.

### ATONY

Atony of the stomach is that condition in which the muscular walls have lost their tonicity, with a resultant motor insufficiency, in consequence of which the stomach is unable to pass its contents into the intestine at the normal rate. Although this condition has long been recognized, great confusion still exists concerning its significance. By some authors it is classified as a purely nervous disorder, by others as a form of gastrectasis, while some pass it by in a cursory manner. Kussmaul<sup>1</sup> was among the first to make a distinction between atony and dilatation. He showed that in gastrectasia due to stenosis of the pylorus or of the duodenum, vomiting is very frequent during the entire course of the disease and is a characteristic sign, while in atony it rarely occurs. Oser<sup>2</sup> attempted to distinguish between dilatation and atony, and stated that in actual dilatation lavage is of great benefit, but that in atony it is of little value. Naunyn<sup>3</sup> laid stress on fermentation in dilatation of the stomach, and showed that in muscular insufficiency fermentation is usually produced. Minor forms without fermentation, he believes, should be excluded from the chapter of true gastrectasia. For clearer views concerning this subject we are much indebted to Boas,<sup>4</sup> who described this disorder at length as a separate pathological condition, devoting a special chapter to it and calling it myasthenia (muscle weakness) or muscular insufficiency of the first degree.

**Etiology.**—As regards causation, atony may be of two kinds, primary and secondary. Primary atony is found in persons who have been in the habit of consuming large quantities of indigestible food; the excessive use of fluids especially predisposes to this disorder; frequently, however, no such cause is assignable. Atony may be secondary to many other

<sup>1</sup> *Volkman's klinische Vorträge*, 1880, Nr. 181.

<sup>2</sup> *Ursachen der Magenerweiterung, Wiener Klinik*, 1881.

<sup>3</sup> *Deut. Archiv f. klin. Med.*, Bd. xxxi, 1882, S. 225.

<sup>4</sup> *Specielle Diagnostik und Therapie der Magenkrankh.*, ii Theil, iv Auflage, S. 89.

diseases, such as those of the brain and cord, typhoid fever, anemia, tuberculosis, and diseases of the gastro-intestinal tract, such as gastrop-tosis, enteroptosis, chronic constipation, chronic gastritis, and nervous dyspepsia. Cholelithiasis is not an infrequent cause (Boas). According to Peyer, it is often found as a neurosis secondary to disease of the generative organs in males. Bamberger finds it frequently congenital, and according to Zweifel it is not uncommon in children, due in many cases to improper feeding. Pfungen has shown that atony of the stomach often originates during the period of puberty. It is not improbable that the precocious appetite at this age, leading to the consumption of much indigestible food, is the cause. No age seems to be exempt and it appears with equal frequency in males and females. In the series of 1592 cases there were 147 cases of atony of the stomach (9.25 per cent.), 79 being females and 68 males. As to age, 7 were in the first decade, 26 in the second, 26 in the third, 30 in the fourth, 25 in the fifth, 19 in the sixth, and 14 in the seventh.

**Symptoms.**—Most patients complain of a loss of appetite, although in rare instances the appetite may be fully maintained, at least in the first stages. When the condition is secondary to nervous disorders the appetite may even be increased (Peyer). A feeling of pressure or fulness comes on, usually during or after meals, and this is especially marked after the ingestion of fluids. In light forms the distress reaches its height immediately after meals, and gradually passes off during the next hour, to be again aggravated by the smallest amount of food. In severer forms it may be so great as to continue with intensity for hours after meals, and become still more aggravated when food is taken again. This feeling of pressure is accompanied by heart-burn, pyrosis, and eructations of gas, but rarely by vomiting. The quality as well as the quantity of food ingested is productive of this symptom; fluids are most likely to induce pressure. Constipation is almost a constant feature, and headache of a dull character is often present and may at times lead to actual vertigo. Nervous symptoms of various kinds may be present, such as palpitation of the heart and indefinite pains, and on this account the disorder is frequently mistaken for neurasthenia.

On physical examination the stomach is found to be enlarged, so that the greater curvature reaches to or below the level of the umbilicus. Peristaltic and antiperistaltic movements of the walls of the stomach may occasionally become visible. With but small quantities of fluid (from 250 to 300 cc.) in the stomach, splashing sounds may be readily produced. In atony the stomach is not only enlarged but its motor function is also markedly impaired, and it does not propel its food into the intestine at the normal rate. Under normal conditions the stomach will be found empty in from six to seven hours. Should particles of food still be present after this time the motor function of the stomach is much impaired. A most important test is the condition of the stomach before the ingestion of food (Boas). If the contents of the stomach be expressed in the morning before taking food, the stomach will be found entirely empty and free from all food remains. This is not so in cases of gastrectasia, in which greater or smaller quantities of food will be



found. Boas has devised still another test which has proved of great service. The test supper of Boas consists of white bread with butter, cold meat, and two cups of tea taken at 8 p.m. In atonic conditions the stomach will be empty the next morning, but in gastrectasis it will still contain food remains at that time.

Examination of the gastric contents is of great importance. The expression one hour after an Ewald test breakfast shows large quantities of solid contents, not separating into the characteristic three-layered fluid of gastrectasis and not containing yeast spores or sarcinæ. Upon chemical examination the contents show in most cases a normal proportion of hydrochloric acid, pepsin, and casein ferment. According to Boas, at the very beginning of atony of the stomach, through constant mechanical irritation of food upon the walls of the stomach, an increased acid production results; in fact, the irritation may be so great that even hypersecretion may be produced. In other cases there may be a condition of subacidity. The findings in this series were hyperacidity, 36; normal acidity, 60; subacidity, 20; anacidity, 14; and alternating acidity in 17.

Among the frequent complications may be mentioned dislocation of the stomach (gastroptosis), of the bowel (enteroptosis), and of the right kidney. Litten endeavored to demonstrate that dilatation of the stomach may cause the liver to move downward, carrying with it the right kidney, but very few accept this explanation and Nothnagel claimed that Litten's cases were for the most part really atony. Although dislocation of the right kidney is quite commonly associated with atony, he maintained that this association was merely a coincidence. It is probable that the atony in these cases is secondary to a gastroptosis. Atony of the intestine is not an infrequent concomitant of atony of the stomach; indeed, both may be present for years, and it may be difficult to tell which is the primary trouble. Gastric vertigo, the vertigo dyspeptica of Trousseau, which this writer believed to be caused by chronic gastritis, probably depends in most cases upon atony (Boas). According to Boas<sup>1</sup> the so-called asthma dyspepticum is not uncommonly found in atony of the stomach.

**Diagnosis.**—Atony must be differentiated from nervous dyspepsia and gastrectasis. According to Bamberger<sup>2</sup> the variability and rapid change of symptoms, the presence of other nervous symptoms, the normal and increased appetite, and the absence and rapid disappearance of the gastric disturbance, distinguish nervous dyspepsia from atony. At times a diagnosis is difficult and sometimes impossible. It must not be forgotten that atony is frequently a complication of nervous disorders.

From gastrectasia, atony is diagnosed by the absence of food remains in the stomach in the morning before taking food; by the absence of the three-layered fluid of gastrectasia, and by the absence of sarcinæ and yeast spores. There is a marked diminution in the secretion of urine in gastrectasia but not in atony.

**Prognosis.**—Atony of the stomach is a chronic disorder and may last for years. It is quite amenable to treatment, and, although it may not

<sup>1</sup> *Archiv f. Verdauungskr.*, 1896, Bd. ii, S. 444.

<sup>2</sup> *Krankh. der Chylopoet. Systems, Virchows Handbuch*, Bd. vii, I, 1855, p. 270.

be perfectly cured, the patient may be relieved of all suffering. It may pass into gastrectasia years after, but this is a rather rare occurrence.

**Treatment.**—Since atony is frequently caused by injudicious and too rapid eating, people with feeble digestive powers should exercise special caution to eat slowly, masticate thoroughly, and avoid indigestible food. Persons suffering from atony of the stomach should eat small quantities of food at frequent intervals. Since water is not absorbed in the stomach to any extent, it is advisable that the quantity of fluids taken should not exceed  $1\frac{1}{2}$  liters a day; this amount should include all fluids. If the thirst is very great, enemata of water may be administered.

The use of milk in large quantities has been recommended, but is not to be advised when the patient is able to go about, since the weight of large quantities of milk may overdistend the stomach; when, however, a rest cure is instituted, milk is often well borne, even in very large quantities. The diet in atony of the stomach varies according to the nature of the gastric secretion. In cases of superacidity a liberal meat diet, consisting especially of chicken, beef, mutton, is recommended; fish, eggs, hard and soft boiled, are also permissible; the vegetables should be selected with care; carrots, peas, and cauliflower may be given, but must be mashed and strained so as to rid them of cellulose. Potatoes, rice, and grits are also allowed. Butter is the best form of fat.

Alcoholic stimulants are, as a rule, not well borne, and their use should be prohibited; in a limited number of cases alcohol in the form of a light wine acts as a stomachic and may be prescribed. In those cases in which there is an absence or a diminution of acid in the gastric secretion the lighter forms of meat, such as the white meat of chicken or fish, sweetbreads, stewed chicken, or raw scraped beef, should be allowed; vegetables, on the other hand, must be given in somewhat larger quantities. The treatment of chronic constipation requires special mention. In the treatment the main reliance must be placed on the diet. Such forms of food should be given as in the course of digestion produce substances to excite intestinal peristalsis; among these foods are Graham bread, certain vegetables, such as carrots, beans, tomatoes, peas, turnips, macaroni, stewed and raw fruits, buttermilk, honey, and cider. This form of diet will often overcome the constipation without the aid of drugs. When the treatment just described proves ineffectual, injections of various kinds, especially of oil, may prove beneficial.

In atony lavage is quite superfluous, and is not to be recommended. The use of the stomach douche is of greater benefit, especially in those cases depending upon the various gastric neuroses. Still more beneficial is the use of electricity, which may be applied either extraventricularly or intraventricularly. The best results are obtained by the intraventricular method. The tonicity of the muscular walls of the stomach is influenced by the faradic current. Painful conditions are alleviated by the galvanic current, the cathode being used intraventricularly, the anode placed upon the fundus of the stomach. To this may be added massage of the abdomen, the effect of which is to increase the peristalsis of the intestine and to strengthen the abdominal walls. In regard to the medicinal treatment, preparations of strychnine seem to serve the

best purpose. Either strychnine sulphate or the extract of *nux vomica* may be given in pill form. To allay the feeling of pressure, which is a constant and annoying symptom, the extract of belladonna is prescribed. When there is a diminished secretion of hydrochloric acid, 15-drop doses of dilute hydrochloric acid, given according to the method of Ewald several times after meals, is indicated. In cases of increased acidity, sodium bicarbonate should be ordered after meals.

### **POLYSYMPTOMATIC NEUROSES. NERVOUS DYSPESIA (LEUBE) OR NEURASTHENIA GASTRICA (EWALD)**

The polysymptomatic neuroses are characterized according to Boas by the presence of an unusual multiplicity of symptoms, in contradistinction to the monosymptomatic forms, in which one symptom is prominent or alone observed. The most important and typical example of a polysymptomatic neurosis is nervous dyspepsia, in which the symptoms are manifold and yet no organic changes can be detected. According to Leube's original conception, the term nervous dyspepsia was intended to cover that group of cases in which the secretory and motor functions of the stomach were normal while the patient was suffering from manifold subjective symptoms following the ingestion of food. More recently Leube included in this class a group of cases manifesting changes in the gastric secretion and motility.

There are two forms of nervous dyspepsia: (1) That in which no anatomical changes can be detected in the stomach. (2) That in which the nerves supplying the stomach are involved in anatomical changes, together with consequent changes in the gastric secretion. Boas describes a third form originating "reflexly from other organs, such as from the kidneys, uterus, ovaries, male generative organs, and particularly in the intestines." In addition constitutional diseases, such as diabetes, tuberculosis, and syphilis may form a basis for the production of this condition. Nervous dyspepsia is also characterized by the fact that all the functions of the stomach, motor, secretory, and sensory may be disturbed at the same time. It is a well-known fact that nervous dyspepsia, accompanying organic diseases of the stomach, can be so combined with it that a most careful investigation may be necessary in order to differentiate between the primary and secondary affection.

**Etiology.**—As nervous dyspepsia is frequently associated with general neurasthenia, all conditions bearing an etiological relationship to neurasthenia are causative in the production of this disorder. A large number are due to worry, anxiety, reverses, overwork, sexual and alcoholic excesses, and also to the abuse of tea, coffee, and tobacco. Certain cases come from diseases of the blood, constitutional diseases or such other diseases as pulmonary tuberculosis and diabetes; other cases occur reflexly, the primary cause being eye-strain, genito-urinary disturbances, mental disturbances, or the puerperal state. In this series of 1952 cases of functional gastric disorders there are 268 (16.5 per cent.) cases of nervous dyspepsia, 154 being males and 114 females. As to age, 33 were in the second decade, 55 in the third, 55 in the fourth, 68 in the



fifth, 38 in the sixth, and 19 in the seventh. It occurs more frequently in males than in females.

**Pathology.**—In 41 patients suffering with nervous dyspepsia Jurgens<sup>1</sup> discovered a total degeneration of Meissner's and Auerbach's plexuses after death; so that in a certain number of cases there appears to be an anatomical basis for this condition.

**Symptoms.**—It is characterized by the multiplicity of its symptoms, varying greatly in intensity, mode of onset, and frequency. The most prominent sign is the gastric discomfort present after meals, although the distress is not dependent upon the quality and quantity of food ingested, but rather upon mental strain, worry, or excitement. It often happens that the most digestible food causes distress, while the most indigestible food is borne without discomfort. The gastric distress is characterized by pressure, fulness, eructations, distension, flatulency, peculiar sensations in the stomach, and heartburn. One food after another is discarded on account of the discomfort produced by eating until the condition of sitophobia is produced with symptoms of marked inanition. In addition manifestations of neurasthenia are often present, headache, depression, vertigo, palpitation of the heart, lassitude, loss of strength, globus hystericus, and insomnia. The appetite is usually capricious, developing into a bulimia, and followed quite suddenly by complete anorexia. The general condition of the patient is not usually affected, although in some instances the emaciation may be so extreme as to suggest a serious organic disease. The periods of well-being, alternating with those of discomfort, are rather characteristic as also are the variations in the intensity of the symptoms from day to day. The abdomen is usually found sunken, occasionally distended with gas, accumulating often in the region of the cecum and in the colon at the splenic flexure; the abdomen is often tender at the distended areas, but the pain is relieved by the expulsion of the gas. The bowels are, as a rule, constipated.

In the larger proportion of cases the gastric secretion is normal; occasionally there is a subacidity and less often a hyperacidity. A characteristic feature is the fact that when anacidity exists the ferments are not generally diminished in quantity; not infrequently marked variations in the state of the secretions are met with (heterochylia). In this series the gastric analysis showed normal acidity in 163, subacidity in 57, hyperacidity in 35, and heterochylia in 13. As a rule, the motor function remains normal, although occasionally atony of the stomach may occur. In the 268 cases a slight atony existed in 57; a gastropptosis is not infrequently found, it being present in 41 of this series.

**Diagnosis.**—This is made by the absence of all indications of organic disease, together with the general neurasthenic symptoms, associated with the digestive disturbances. It is further strengthened when the motor and secretory functions of the stomach are found normal. Greater difficulty, however, is manifested when these functions are not perfectly normal, but even then the symptoms present are so far out of proportion

<sup>1</sup> *Verhand. des III Congresses f. Medicin*, S. 253.

to the changes that these slight variations will not account for the condition found. The discomfort is not dependent upon the quantity and quality of food; indigestible food does not increase the distress.

It is always necessary to exclude all organic conditions, but this is not always a simple matter. Boas advises the following plan in doubtful cases: A very easily digestible diet is given the patient, similar to that ordered during the third week of an ulcer treatment; while on this diet, the subjective symptoms are observed for a period of from three to four days, when other foods are gradually added, such as sauces, vegetables, desserts, and various fruits. The symptoms are now compared with those during the first period. In nervous conditions they do not increase in intensity on the fuller diet but will often lessen, while in organic disease they will increase.

Nervous dyspepsia is distinguished from *chronic gastritis* in that the gastric disturbance is more or less directly dependent upon the quality and quantity of food ingested in the latter condition, while the gastric contents contain large amounts of mucus not observed in nervous dyspepsia. There may be an absence of free hydrochloric acid in both disorders, but an absence of enzymes does not usually occur in nervous dyspepsia. It is differentiated from *ulcer* by the absence of a localized, painful area in the epigastrium which, although it may be present for a few days at a time, is not constant; by the absence of hematemesis and occult blood in the stools and by the sudden disappearance of all discomfort. Often the diagnosis can only be made after trying the effect of an ulcer cure.

In a certain number of cases of nervous dyspepsia the emaciation is so intense as to suggest *carcinoma*, especially if at the same time there is an absence of free hydrochloric acid. A correct diagnosis is arrived at by noting the age, the duration of the disorder, and determining the presence or absence of a motor insufficiency as well as of occult blood in the feces. The condition under discussion is further distinguished from gastric atony by the rapid changes in symptoms, and the non-dependence of discomfort on the quantity and quality of food ingested; atony and nervous dyspepsia are at times so combined that it is impossible to determine which is the primary disorder.

**Prognosis.**—This is not always favorable, although, as a rule, it is not a fatal disease. It may become rather obstinate and resist all attempts at treatment; the milder forms usually yield readily to proper treatment, while the severer ones continue over a long period of time before entire relief is afforded or may show rapid loss of flesh and strength and finally end fatally. Relapses are not uncommon.

**Treatment.**—Boas has made the statement that “in the larger proportion of cases of nervous dyspepsia drugs are not indicated. The patient should be taught that recovery cannot be brought about by the use of drugs, but only by a sensible mode of living and following the laws of hygiene.” In all cases in which it is possible to determine the cause, this should be relieved, *i. e.*, all intestinal disturbances should be corrected, anxieties and worries relieved, and sexual disorders treated. When no cause can be determined, the treatment should be directed toward the

general neurasthenia. This is often best combated by change of scene and climate. The diet should not be too restricted, but strengthening food, without any attempt at a too rigorous diet, should be prescribed. In those cases in which milk is well tolerated it may be given in large quantities; when it is not well borne, buttermilk, kefir, or koumyss may be substituted. The patient's appetite is humored, and he may be allowed to eat any food he can digest. Alcoholic stimulants are prohibited, or given only in very small quantities. In severe cases a well-conducted rest cure will produce the best results. In those cases in which the patient has lost much flesh and strength, the most beneficial results are obtained by these means with forced feeding and isolation. Hydrotherapy, massage, and electricity are useful. Rosenheim has recommended the gastric douche, while others practice lavage. Of the medicinal remedies used the milder preparations of iron, arsenic, bromides, and the preparations of valerian must be noted.

## SUMMARY OF 1592 CASES OF GASTRIC NEUROSES

## MONOSYMPTOMATIC GASTRIC NEUROSES

*Irritative Group*

	Cases.	Per cent.	Males.	Females.
Superacidity or hyperchlorhydria . . . . .	542	34.00	263	279
Supersecretion: Intermittent . . . . .	21	1.50	15	6
Continuous . . . . .	10	0.65	7	3
Digestive . . . . .	2	0.10	2	0
Bulimia . . . . .	24	1.50	5	19
Parorexia . . . . .	8	0.50	2	6
Gastralgokenosis . . . . .	7	1.50	7	0
Hyperesthesia . . . . .	31	1.50	4	27
Gastralgia . . . . .	24	2.00	7	17
Rumination or merycism . . . . .	24	2.00	20	4
Regurgitation . . . . .	32	2.00	26	6
Eructatio nervosa . . . . .	54	4.00	12	42
Vomitus nervosus . . . . .	49	3.00	15	34
Nausea nervosa . . . . .	40	2.50	10	30
Cardiospasm . . . . .	25	1.50	8	17
Pylorospasm . . . . .	4	0.30	1	3
Pneumatosis . . . . .	8	0.50	6	2
Peristaltic unrest . . . . .	1	0.06	1	0
	906	57.61	411 (26%)	495 (31%)

*Depressive Group*

	Cases.	Per cent.	Males.	Females
Subacidity or hypochlorhydria . . . . .	80	0.5	34	46
Anacidity or achylia gastrica . . . . .	112	0.7	55	57
Akoria . . . . .	5	0.3	3	2
Anorexia . . . . .	48	3.0	11	37
Sitophobia . . . . .	24	1.5	6	18
Incontinence of the pylorus . . . . .	2	0.1	1	1
Atony . . . . .	147	9.25	68	79
	418	26.15	178 (11%)	240 (15%)

## POLYSYMPTOMATIC GASTRIC NEUROSES

	Cases.	Per cent.	Males.	Females.
Nervous dyspepsia . . . . .	268	16.5	154 (9.5%)	114 (7%)



## CHAPTER V

### ORGANIC DISEASES OF THE STOMACH

By CHARLES F. MARTIN, M.D.

#### GASTRIC AND DUODENAL ULCER

**Synonyms.**—Simple ulcer of the stomach; round ulcer; peptic ulcer; chronic ulcer; perforating ulcer; *ulcus ventriculi* (Frank); Cruveilhier's disease (Cruveilhier was the first to give a good clinical and anatomical description of the condition). The first name is doubtless the best, for these ulcers are not always round, neither are they always chronic, nor do they always perforate. Erosions of the gastric mucosa are probably often early conditions of gastric ulcer, both as regards etiology and morbid anatomy, and the subsequent autodigestion affords the more typical appearance of the simple ulcer.

**Definition.**—A more or less progressive destruction, beginning in the mucosa and sometimes extending to and even through the deeper layers of the stomach wall, of the nature of a degeneration or a necrosis. These ulcers occur practically only where the gastric juice flows, and are found, therefore, only at the extreme lower end of the œsophagus, in the stomach itself, and in the portion of the duodenum above the opening of the common bile duct. Such ulcers may be acute or chronic, with or without tendency to cicatrization and healing. They leave an open loss of substance, usually round or oval in shape, with edges which are, as a rule, clean cut in the acute and subacute cases, more irregular in the chronic. Acute exacerbations of chronic ulcers are commonly mistaken for acute ulcers, and the subsidence of the acute period is often mistaken for the cure.

**Statistical.**—Statistics in regard to gastric ulcer are, on the whole, of very doubtful value. Those based upon clinical observation alone are unsatisfactory; because of the difficulties in diagnosis of obscure cases many other conditions are often erroneously included. Statistics, again, bearing upon pathological examinations are often insufficient, either from the frequency with which simple ulcers are overlooked, or because the healing has been so perfect that often, as Bramwell states, no scar at all is left behind. The unsatisfactory grouping of cases of simple round ulcer with those due to causes of an entirely different nature renders the statistics still more unreliable. Combined clinical statistics show 3036 cases diagnosed as ulcer among 339,575 patients, *i. e.*, 0.894 per cent. Combined statistics of autopsies of various series show 2608 ulcers out of 59,450 autopsies, *i. e.*, 4.4 per cent. As a cause of death, ulcer occurred in 410 out of 444,564 deaths.

**Geographical Distribution.**—The regional differences are great, the most marked being, as Rutimeyer has shown, between North America on the one hand (0.12 to 1.28 per cent.) and Central Europe on the other, (0.54 to 3 per cent.) clinically. Their pathological variations are

even more marked (0.85 to 2.35 per cent. as against 1.30 to 11.0 per cent.). For the reasons cited it does not seem possible to obtain useful statistics on regional differences in distribution.

**Etiology and Pathogenesis.**—The three main etiological factors in simple ulcer of the stomach are: (1) An injury to the gastric mucous membrane; (2) a circulatory disturbance; and (3) the acidity of the gastric juice. The combination of these three factors appears to permit of autodigestion. No single well-defined cause has been found. Much has been done to produce ulcers experimentally in the lower animals, but recent observations, particularly those of Kawamura, have shown that they possess a dubious value. It would appear that ulcers of the stomach abound in the greatest variety of conditions in rabbits and they have frequently been found in stomachs that were supposed to have been normal. Experiments on rabbits are unreliable, and those on dogs are open to a great deal of criticism, as it is impossible to determine what the real etiological factors were in the experiments.

**Age.**—Gastric ulcer is most common between twenty and thirty years of age, though the age incidence differs according to the sex. The average for males is 36.7 years and for females 27.1 years of age. In infancy it is rare, no case occurring under ten years in 262 autopsies on cases of ulcer at the Berlin Pathological Institute. Cutler studied 29 cases, of which 6 were found immediately after birth, 8 under seven years of age, and 9 between the ages of eight and thirteen years. Rehn, on the other hand, collected 9 cases of simple ulcer in children, and Kundrat speaks of frequently having found minute pinhead-sized ulcers in children, which, however, were probably the result of hemorrhage and differed thus from ordinary round ulcer. Martha Wollstein, Holt, and others, have added cases, though many experienced pediatricists have never observed a case clinically. The symptoms seem less distinctive than in adults, and depend chiefly on evidences of blood in the vomitus or feces, for which many other causes than ulcer may be found, *e. g.*, hemorrhages from the nose, throat, lungs, or from the mother's breast; or, again, from general constitutional diseases, such as scurvy, purpura, the malignant exanthemata, cirrhosis of the liver, etc. Perforation seems to be relatively more common in children than in adults. Hensch found ulcers occasionally in the newborn, and, according to Osler, they are sometimes found in the fetus. An example of the presence of ulcer at the other extreme of life is reported by Eleanor C. Jones in a man, aged eighty-four years, with a past history of gastric ulcer thirty years before, and in whom, at death, a fresh ulcer was found next to the scar of the old healed ulcer.

Riegel's statistical table (compiled from clinical cases) is interesting:

Age.	Riegel's table.			The writer's combined clinical statistics.	
	Men.	Women.	Total.		
0 to 10 years . . . . .	..	..	..	1	0.14 per cent.
10 to 20 years . . . . .	8	35	43	85	12.00 per cent.
20 to 30 years . . . . .	29	62	91	259	37.00 per cent.
30 to 40 years . . . . .	35	22	57	186	26.50 per cent.
40 to 50 years . . . . .	36	11	47	110	14.00 per cent.
Over 50 years . . . . .	18	4	22	63	9.00 per cent.
Total . . . . .	126	134	260	704	

**Sex.**—Statistics on this point vary greatly and one should not attach too much importance to individual reports. Clinically, most statistics show a preponderance of women over men, in the proportion of 2 or 3 to 1, but, pathologically, the numbers are about equal in both sexes.

**Occupation.**—This bears some relation to ulcer only in so far as injury to the mucosa or the circulation may occur, and no walk of life appears to be exempt. According to some authorities, cooks are predisposed presumably because of their habit of swallowing foods which irritate the mucous membrane. In Payne's statistics only 3 out of 50 females were cooks. Workers in metals (Bouvert), glass and porcelain factories (Bernitz), who are in the habit of swallowing dust particles, are thought by some to be more liable; so also tailors and shoemakers because of their position and occupation leading to abdominal pressure; but in all these there would seem to be some preliminary injury to the mucosa or the circulation.

**Dietetic Errors.**—In themselves these are scarcely to be regarded as the cause of true gastric ulcers except when they create trauma. Where a combination of circumstances may induce hyperacidity, disease of the mucosa, or other conditions, to *assist* formation of gastric ulcer, it may be that indigestible foods or dietetic indiscretions aid the development of the condition, or may be, at least, regarded as antecedents.

**Infections.**—Letulle found gastric ulcer in a man suffering from dysentery and isolated bacteria from the stools, which, when injected in pure cultures into guinea-pigs, produced specific erosions and ulcerations. Erosions and ulcers, however, are frequently found in general infections, and although Martin believes that the pyloric site of ulcer favors the bacterial theory, the anatomical appearances of the ordinary round ulcer scarcely suggest a bacterial origin. *Spirochætæ* may predispose to gastric ulcer by producing vascular changes, but there is no relation between the specific luetic gastric ulcer and the one under consideration. *Tuberculous* ulcers, which seem to be more and more frequently found, are likewise not to be regarded in the category of the ordinary round ulcer. While it may be true that 20 per cent. of patients with ulcer die of tuberculosis, it is equally probable that the underlying conditions which favor the development of gastric ulcer likewise favor the development of the tubercle bacillus. Round ulcer is a pure necrosis and not a pure infection.

**Trauma.**—As a cause of gastric ulcer this may be external or internal. Internal trauma, arising from hot foods, corrosives, foreign bodies, and mechanical and chemical irritants, may produce gastric ulcer or such early lesions as may later lead to ulcer. External injury, as from a blow or, perhaps, even from mere compression, may cause ulcer.

Ritter produced experimental submucous hemorrhage in dogs after inflicting blows on the stomach, in one case causing even a separation of the mucous membrane, and it was his opinion that injuries predisposed to ulcers through the subsequent action of the gastric juice. He further describes an incident in which injury in the epigastric region was followed in eight days by hematemesis and other signs of gastric ulcer. Fertig describes an apparently undoubted case in which, as a result of a kick



in the abdomen, four gastric ulcers were found at autopsy. One may conclude, however, that such injuries sometimes provide the original lesion for the later formation of true ulcer. The same probably holds true of the theory of Rokitansky and Rindfleisch and Key, that ulcers arise from hemorrhage and subsequent erosion.

This seems to be the view taken by Richardière, whose traumatic ulcer cases are classed in two groups, the one, acute cases healing rapidly, the other, cases running a course similar to ordinary chronic ulcer. The difference in the result may depend on the condition of the gastric juice, especially as regards its acidity. Violent emesis as a mechanical factor in the causation of gastric ulcer is a doubtful cause and much more likely to be associated with some underlying condition, such as uremia.

**General Disease.**—Chlorosis and anemia are thought by many to be predisposing factors, while, *vice versa*, chronic ulcer certainly often leads to anemia. Samuel and W. S. Fenwick hold that a definite relation exists between ulcer and anemia, and 72 per cent. of their cases showed symptoms of anemia before serious ulcer symptoms developed. Perhaps, as Cabot and Stengel suggest, the chlorosis is often due to hemorrhages, though in Fenwick's case the chlorosis occurred without these. There can be little doubt that ulcer occurs more commonly among those who are anemic than in persons in perfect health.

*Previous gastric trouble* as an etiological factor is of doubtful importance, except, of course, when hyperacidity and hypersecretion have existed. It is difficult, however, to draw the line between the symptoms of previous gastric disturbances and the early signs of ulcer, for a supposed preliminary gastritis may have been merely the indefinite symptoms induced by the already existing ulcer. C. H. Miller believes that inflammatory swelling and rupture of lymphoid follicles may induce erosions which may probably develop later into true ulcers. Gastric ulcer is essentially a *necrosis*. It is doubtless due primarily to a circulatory disturbance, be it arterial, venous, or capillary, and when once a defect occurs it is prevented from healing by the action of the gastric juice. Excessive acidity makes the ulcer chronic. This tendency to chronicity with lack of healing power is the distinguishing characteristic of simple ulcer as opposed to a mere traumatic erosion.

**Relation of Circulatory Disturbance to Gastric Ulcer.**—Various circulatory disturbances may account for the early changes which produce lesions.

**Arteries.**—*Embolism.*—Virchow, Orth, and recently Payr, insisted on the embolic nature of the disease. Payr's experiments have established the etiological relationship of ulcer with disturbance of the circulation. The fact that the arteries are not terminal implies that ulcer is not the necessary invariable result, and often, too, where ulcer exists, no emboli can be found. The same holds true with thrombosis. Arteriosclerosis comes under the same head (Howard), as, too, would ligature of the afferent vessels (Litthauer).

**Vascular Spasm.**—Contractions of the muscularis mucosa, including the afferent vessels (Talma, Lichtenfeld, Bergmann, Rossle) have also

been associated with gastric ulcer. It is doubtful, however, if contraction of the muscularis mucosa would affect the arterial rather than the venous portal system. Arterial spasm, however, may be accountable for the acute perforating ulcer.

*Venous.*—Hemorrhagic infarction and submucosal hemorrhages from external trauma (Ritter, Fertig, Kronlein), and internal, through chemicals and irritating substances, affect the surface of the projecting folds of the mucous membrane. Aschoff has insisted on the importance of this factor. Whatever the circulatory disturbance may happen to be—and any one of these may institute an early lesion—other factors must be superadded to produce the ordinary ulcer, for without them healing will occur. *The mechanical factor* is of great importance and helps to account for the production of some forms of circulatory disturbances. Aschoff has drawn attention to the early origin of ulcer on the top of folds of the mucous membrane, especially at the lesser curvatures, where two large rugæ exist, exposed to attrition, to contact with thermic, chemical and mechanical causes of injury, as well as to the effects of muscular spasm. There would seem to be certain points in the cavity of the stomach where contact with irritative substances is more constant and where food is retained for a longer period, thus keeping up the irritation. It is at these points, as Aschoff has shown, that ulcer is most frequent.

*Nervous influences* originating in the central nervous system, in the cœliac ganglia, in the splanchnic, the vagus, and elsewhere, play a part which is only subordinate. It is possible that they produce the circulatory disturbance which, later on, develops into an ulcer. The work of Eppinger and Hess, following the suggestions of Bergmann, is of interest. According to these writers the equilibrium between the vagus and sympathetic systems is sometimes disturbed, resulting in spasm of the muscularis mucosa, which helps to produce circulatory disturbance and ulcer. G. v. Bergmann has attempted to show that in cases of gastric ulcer there are already various stigmata to show this want of harmony, *e. g.*, hypersecretion, spastic contractility of the muscles, spastic constipation, cold extremities, and other evidences of the so-called neuroses.

**The Relation of Hyperacidity and Hypersecretion to Gastric Ulcer.**—Statistics vary regarding the frequency of hyperacidity in gastric ulcer. This may be due, in part, to faulty observations, but for the most part to a difference in interpretation of what hyperacidity and hypersecretion really mean. It would seem that in a large proportion of ulcer cases increased secretion of hydrochloric acid is found; in many others, however, repeated examinations have shown that the acidity is either normal or deficient. Einhorn, in America, found hyperacidity a common feature of gastric ulcer, as did also Robin in France, and Fenwick in England. Rutimeyer, however, in 162 cases (36 men, 126 women) found 42.5 per cent. with hyperacidity, and 57.4 per cent. with the acidity normal or diminished. Hyperacidity was relatively much more frequent in men. It is, however, thought that in gastric ulcer the symptoms of hyperacidity arise through the delay in neutralizing the acid contents discharged into

the duodenum. This results in pylorospasm, which in its turn produces retention of secretion and the condition known as Reichmann's disease. Bickel has demonstrated that the proportional quantity of acid secreted in the gastric juice is, under all conditions, uniformly the same; hence the presence of excessive acidity means the presence of excessive secretion in general.

In the present state of our knowledge the following views may be regarded as justifiable:

1. Hypersecretion and hyperacidity are common in gastric ulcer, though not essential to the diagnosis. Gastric ulcer, however, occurs only where gastric juice flows.

2. The amount of secretion and acidity vary at different stages and periods of the disease. Hyperacidity often appears at the time immediately preceding or following a hemorrhage; many exceptions to this occur.

3. Hyperacidity occurs in the absence of gastric ulcer, but when persistent it should suggest the diagnosis of ulcer.

4. Hyperacidity alone cannot produce gastric ulcer.

5. The frequent association with chlorosis makes the combination an important factor in the etiology.

6. Hyperacidity superadded to a lesion of the mucous membrane is an important etiological factor.

7. Hyperacidity may induce gastric ulcer when through any cause a portion of the mucosa is injured. This may occur in two ways: through direct contact with the acid, and by its action on the exposed vessels, which are thereby contracted, and a local anemia and necrosis thus induced.

8. That chronicity is directly induced by hyperacidity is responsible for the prolonged course of the disease, and prevents healing. It does not form ulcers often, but causes them to become chronic.

9. The failure of many cases in which gastro-enterostomy has been performed is probably associated with hyperacidity and hypersecretion.

**Pathology.—Situation.**—These ulcers exist wherever the gastric juice flows. The posterior surface of the stomach is the commonest site, and ulcers are found there in 42 per cent. of all cases, especially near the pylorus and along the lesser curvature. The situations are variously described. In statistics of over 2000 cases collected from various sources the following percentage occurred:

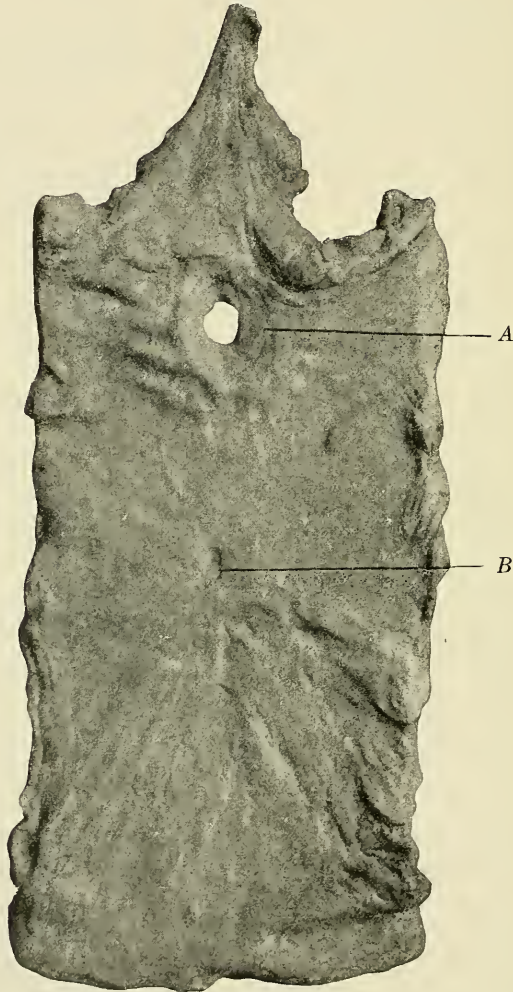
On the lesser curvature . . . . .	726 or 35.0	per cent.
Posterior wall . . . . .	585 or 28.0	per cent.
Pylorus . . . . .	291 or 14.0	per cent.
Anterior wall . . . . .	182 or 9.0	per cent.
Cardia . . . . .	134 or 6.5	per cent.
Fundus . . . . .	62 or 3.0	per cent.
Greater curvature . . . . .	75 or 3.6	per cent.
Anterior and posterior walls together . . . . .	14 or 0.7	per cent.
Total . . . . .	2069	

**Number.**—These ulcers are usually single, but often multiple. Indeed, that they are commonly multiple is becoming more and more recognized.



There were 34 in one of Berthold's cases. Sometimes a perforated ulcer is found at operation and after healing another may perforate. In Brinton's 463 cases, 381 had one ulcer, 57 showed two ulcers, 16 had three, 3 had four, 2 had five ulcers, and 4 had more than five. When multiple, they may all seem to be of the same duration, or some may be

FIG. 2



Two gastric ulcers: *A*, showing a shelving base and central perforation; *B*, more superficial.

in a state of healing, while others seem to be quite recent. Welch and others regard 20 per cent. of cases as multiple. In 13 out of 21 cases operated on and resulting fatally, Carless found more than one ulcer. Sometimes one ulcer is in the stomach and another in the duodenum.

**Shape.**—The more acute ulcers are punched out in appearance, round or oval and sharp in outline, while the less acute ones are shelved or

terraced, the widest diameter and the greatest loss of substance being at the mucosa. The ulcers become gradually narrower as one approaches the serosa (funnel-like, Aschoff). This was seen to correspond to the distribution of the bloodvessels, and Orth had drawn attention to this fact. The still older lesions are often irregular in outline, spread out, and with the mucosa rolled inward and thickened at the edges. If extensive, they are serpiginous, especially where several have fused. Thickening and raising of the edges occur as the ulcer gets older. Often they are saucer-like, with bevelled edges, and rounded out or concave.

*Cicatrization* may often be seen progressing in various portions of the walls. The muscle beneath is shrunken, the floor is smooth and grayish, brown or red, rarely ragged. It is generally covered with some necrotic tissue, and in old ulcers with indolent granulation tissue. Sometimes there is a hemorrhagic exudate. Adhesions externally and scarring within cause deformities in the organ (hour-glass stomach, etc.).

**Size.**—The usual size varies from 2 cm. to 3 to 4 cm. in diameter; in many instances, however, they may be as small as 1 cm. or less, or, again, as large as 10 cm. in diameter, sometimes even forming a ring more or less completely surrounding the organ. Peabody records one measuring 19 by 10 cm.

**Histology.**—The lesion is essentially a necrosis. There is very little inflammation or sign of healing in acute round ulcers, and even in many older ones; hence the slow repair, resembling somewhat the *ulcus perforans pedis*. There are, moreover, some signs of digestion.

**Healing and Cicatrization.**—Undoubtedly many ulcers occur and heal without giving symptoms of any kind. Many are superficial erosions rather than ulcers and healing occurs with granulations from the sub-mucosa and scar formation. At all events, the frequent presence of scars and little fibroid areas suggests the possibility of ulcer as the cause of these. The healing process commences from the sides and floor of the ulcer. There is proliferation of the adjoining fibrous and glandular tissues, the edges become indurated, and the margins are more indefinite and irregular in outline, with signs of puckering and contraction. The gland structures are repaired to a limited extent only; the new tubules are small and atypical, not like the original epithelial structures, but with cylindrical cells often arranged around the lumen, with no opening toward the stomach cavity and no secretion from the cells. Sometimes in old ulcers the healing process leaves chronic inflammatory areas which tend to erosion and recurrent bleeding. The area of stomach around old ulcers is often infiltrated with small cells and fibroblasts to a great extent. Where muscle tissue is lost it is replaced by fibrous tissue.

*Scars* vary in size, and, according to their size and situation and to the amount of contraction which follows the healing process, they may or may not cause perceptible deformities in the organ and corresponding functional disturbance. The deformities thus caused comprise hour-glass contraction, pyloric stenosis and gastrectasis, and other irregularities with or without obstruction. Perforation occurs when the ulcer penetrates down to the serosa before adhesions have formed, and for this reason it naturally occurs most commonly on the anterior wall.

**Symptoms.—Latency.**—There may be no characteristic symptoms, and the first discovery of a gastric ulcer may be made unexpectedly at autopsy. Stoll found it latent in 27 per cent. of his autopsies; Lebert found that 15 per cent. of 110 cases were latent until severe symptoms arose. Then, again, the first evidence may be a sudden or perhaps fatal hemorrhage, or the peritonitis following a perforation. It may be latent, even if perforation has taken place, as in one instance in which an ulcer giving suspicious signs of perforation remained quiescent. The patient for some days after the event seemed to improve, and there was little or no tenderness in the abdomen. Several weeks later an abscess developed in the pelvis, which was opened per vaginam and drained, and the autopsy revealed the origin to be in a fistulous opening from a perforated gastric ulcer. Sometimes nothing but *backache* occurs, as in the case of Beneke, in which for years this was the only symptom; a sudden peritonitis from perforation caused death and the autopsy showed old adhesions to the liver and a perforation between the adhesions into the abdominal cavity. Sometimes spinal disease is suspected, and a plaster jacket has been put on.

**Dyspepsia.**—While the cardinal signs are pain after eating, epigastric tenderness, vomiting, and hematemesis, yet often, perhaps even as a rule, the symptoms are less definite and *dyspepsia* is the only evidence to be found, with perhaps a little vomiting or regurgitation. There may be a sense of fullness, weight, or distension with gaseous eructations. With these there may be pyrosis, occurring during the digestive period, or mere gnawing or burning or "*heissshunger*" (from hyperacidity). Orthoform has been used as a test, dulling the sensitive exposed areas of ulcers and having no effect on mere hyperesthetic mucous membranes. Its use, however, has justly been called into question, as its action is unreliable. The general condition of the patient, as a rule, remains good, although anemia, emaciation, and weakness, all due to local causes in the stomach, are common and sometimes marked. Nervousness, melancholia, headache, and dizziness are frequent; so, too, are amenorrhœa and dysmenorrhœa. Fever is usually absent, unless complications arise (peritonitis, hemorrhage, etc.). Often there may be a rise of  $1^{\circ}$  without complications, perhaps associated with anemia. The appetite varies; it may be excessive, but the patient fears to eat because of pain. Thirst is common. Constipation is the rule because of sex, food, anemia, lack of exercise, and vomiting. The stools may show blood.

The urine is lessened in quantity when vomiting occurs or when less nourishment is taken. It is usually less acid than normal, especially when gastric hyperacidity is present. Indeed, it is often alkaline, more particularly if gastrectasis be present, and then, if there is fermentation in the stomach, the urine will show an excess of ethereal sulphates and indican. Acetone and diacetic acid are sometimes present, and one may even find serious acidosis. Other alterations are unimportant. Sometimes there is albumin, and this is not uncommon after severe pain. Dreschfeld found albumoses occasionally present.

**Special Symptoms.—Pain.**—This may exist in all degrees from a slight discomfort due to hyperacidity, to acute agonizing paroxysms. It may



be relieved or aggravated by food. Pain occurs in over 90 per cent. of all cases. Intermittency of the pain is one of its most characteristic features. It is frequently localized and nearly always referred to the same spot in the epigastrium below the xiphoid cartilage. Pressure of the hand or clothing usually aggravates it. It may or may not be altered by a change of posture. One may say, as a general rule, that the effects of posture give no clue to the site of the ulcer.

*Time of Appearance.*—Pain occurs during the digestive period either at once after taking food, or at the height of digestion, two to four hours after; the hyperacidity increases it.

*Site.*—The pain is usually in the epigastrium—high up—and may be to the right or left of the median line, though the tenderness is more to the right side as a rule. According to French writers, two points of pain exist: (1) Visceral pain corresponding to the injured area, occurring late in the disease and only with perigastritis; and (2) solar pain—epigastric and not characteristic of ulcer; it is equally common in other diseases. Not infrequently a tender point is found in the back, 2 to 3 cm. to the left of the vertebral column, somewhere between the seventh to twelfth dorsal vertebræ.

*Effect of Food upon Pain.*—It is distinctly aggravated by a large amount of solid food, but there are exceptions in which food sometimes gives relief, especially albuminous food, if there be hyperacidity. Sometimes, too, there is no relation whatever between the food ingested and the onset of the pain. Rutimeyer found this to be the case in 14 per cent. of his 200 cases. The pain is often relieved by rectal alimentation.

The *cause* of the pain varies, it being apparently due sometimes to food, sometimes to the gastric movements or to involvement of the peritoneum. Scars do not usually cause pain unless there are adhesions. J. Mackenzie holds that it is a viscerosensory reflex—a referred pain—and that the tenderness depends on muscular and cutaneous conditions rather than on the organic change in the stomach itself.

*Vomiting* is perhaps less constant than the pain. Cantlie found vomiting in 79 out of 85 of his cases in Montreal. There may be merely nausea and flatulence without vomiting, or, again, the vomiting may appear only at intervals of a week or more. It has a very definite relation to pain, by which it is usually preceded. There is often no nausea, as one might naturally expect if the pain is the chief cause. It occurs sometimes immediately after taking food, but usually one, two, or three hours later, that is, during digestion and generally at its height. The pain is usually relieved by it. In some cases the vomiting may depend on infection from the mouth through the swallowing of bacteria. In more or less acute ulcer there are no signs of motor insufficiency, and the vomitus consists merely of the food taken; in the older ulcers, when perhaps pyloric obstruction has already occurred and the stomach is dilated, the usual vomitus of motor insufficiency and gastrectasis may be present. As hyperacidity is usually present, one finds, as a rule, that digestion is quick and the albumins are well divided, although at other times the food is quite undigested and the vomitus acid.

*Hematemesis.*—Blood is frequently present in the vomitus, and occurred in more than 25 per cent. of all cases of gastric ulcer at the Royal Victoria Hospital. It is well to remember, in this connection, the many other causes of hematemesis that may exist, especially erosions of the mucosa. The source of the blood in gastric ulcer may be venous, arterial, or capillary. Savariaud found in 54 cases that the hemorrhage was venous in 4, from the splenic artery in 17, from the coronary artery in 6, from the pancreatico-duodenalis in 7, from the gastric arteries in 10, while in 10 others the source was undetermined. Sometimes the bleeding is more latent, being not visible to the naked eye either in the vomitus or feces, although minuter methods of detection reveal its presence. These "occult bleedings" have considerable importance in diagnosis.

One cannot always tell the actual vascular sources from the amount of blood. The hemorrhage may be severe or slight. It may be fatal at once, even before ejection from the stomach, the "hemorrhagie foudroyante," when a large artery is eroded; or there may be repeated small hemorrhages. Hemorrhage is responsible for about 20 per cent. of all the deaths in ulcer.

*Symptoms and Signs of Hematemesis.*—The hemorrhage comes on usually after meals, subsequent to some effort or strain, such as from vomiting or defecation. Usually when there is a serious hemorrhage, the patient vomits a large amount of bloody fluid, becomes pale, cold and clammy, complains of dizziness, is often semi-conscious or more or less collapsed. Headache and thirst follow. The pulse is rapid and small, and there is dyspnoea or sighing, and often complaint of a warm feeling in the epigastrium. If recovery occurs, the reaction is apt to come on with fever. The vomited blood may be bright or dark in color, bright if the vomiting be arterial, copious, and rapidly following upon the escape of the blood from the vessel, because the corpuscles are comparatively unchanged. It is more usually dark red, sometimes brown, resembling coffee-grounds, the hemoglobin having been changed to methemoglobin by the hydrochloric acid, and few corpuscles are left unaltered. The vomitus, which may be copious, contains coagula, bits of food, is usually acid in reaction, and devoid of froth. There may be lesser repetitions of the hemorrhage, or after the one large one there may be spontaneous cessation. Hemorrhage may be divided into that from the acute and that from the chronic ulcer.

In the *acute ulcer* there may be a spontaneous, abrupt, and alarming onset, without previous warning and history. Much blood is lost quickly, and the patient either soon dies or the hemorrhage ceases of itself, with only slight repetitions and with anemia; or there may be an abrupt onset, with short intermissions before one or more recurrences. In *chronic ulcer*, on the other hand, the hemorrhage varies much. There is a history of chronic indigestion with vomiting for some time previously, and of persistent anemia.

Moynihan divided these cases into four groups: (1) The hemorrhages which are latent and insignificant. (2) Those which are intermittent, infrequent, and moderate in amount. There is no danger in these of a fatal issue. (3) Those which have become worse after the symptoms

have developed. The bleeding may be copious and repeated, and, therefore, perilous, perhaps even fatal. (4) Those cases in which the hemorrhage is sudden, overwhelming, and fatal. Sometimes the hemorrhage is repeated in spite of care, and, according to Moynihan, is attributable to distension of the stomach and stretching of the ulcer. Some of the blood reaches the intestines, and during the next day or two the feces are black or brownish-black with a shiny surface. It does not, apparently, require a great deal of blood to produce a tarry stool, although Hosslin, quoted by Howard, states that 500 cc. are necessary. Sometimes the color is brighter, depending on the freshness of the blood, the amount, the rapidity of bleeding, and on its passing with the intestinal contents. The discoloration is due to the intimate mixing of the blood and chyme in the small intestines. Sometimes all the blood escapes per rectum, and there is no hematemesis; this occurs when the bleeding is more gradual or the ulcer near the duodenum.

*"Occult Bleeding."*—Strauss first drew attention to this valuable sign, and, in 1902, Boas showed the diagnostic significance of the constant presence of occult blood in cancer of the stomach, and, following upon his observations, others have recorded their experiences, all of which tend to show that the examination of gastric contents, vomitus, or feces for evidences of hemorrhage and its underlying cause has considerable diagnostic value. It is a well-recognized fact that much blood may be present in the feces and yet go undetected, owing to alterations in its color and the nature of the diet administered.

The examination for occult hemorrhages must, of course, be preceded by the exclusion of all other sources of blood, *e. g.*, food containing blood, bleeding from the gums or nose, injuries to the gastric or œsophageal mucous membrane from passing a tube (in which cases, however, the bright-red blood is obvious to the naked eye), general or systemic diseases, and diseases of the digestive organs. Of the general systemic diseases, one considers especially hemophilia, purpura, scurvy, typhoid fever, arteriosclerosis, and tabes with gastric crises. There are two other classes of diseases of the alimentary tract in which this symptom may appear and give rise to some confusion in the diagnosis: (1) Malignant tumors of the gastro-intestinal tract and of the pancreas or liver with ulceration, and also hemorrhagic pancreatitis. These give marked and often constant reactions. (2) Stenosing gastritis, alcoholic gastritis, polypi, intestinal parasites, tuberculosis, syphilitic or simple catarrhal ulceration of the bowel—also hemorrhoids, fistula, and fissure. All of these give constant and marked reactions. The ingestion of much raw or ill-cooked beef (200 gm.), blood sausage, etc., will likewise give positive reactions.

Extreme care in the preliminary dieting for these tests is unnecessary, for, as a matter of fact, there are but a few meats which yield positive reactions (*e. g.*, the above-mentioned raw, minced beef and rich beef-steak and blood sausages), and the quantity must be over 200 grams. Well-boiled or roasted meat does not interfere with the tests. In suspected cases it is especially useful to examine the feces for the presence of blood after pain has occurred.



*The Benzidin Test.*—This is probably the most suitable of all the chemical tests. First used by the Adlers in 1904, benzidin, one of the diphenyl group, has been recognized as the most delicate test hitherto employed for the detection of occult blood, giving positive results in blood dilutions of 0.001 per cent. The quality of the benzidin is of importance for its delicacy of reaction. The test as modified by Schlesinger and Holst is as follows: A “knife-pointful” of benzidin is added to 2 cc. of glacial acetic acid in a clean test tube. A solution quickly ensues after shaking. In another test tube a tiny portion of feces (the size of a pea) is well mixed with 2 cc. of water, and heated to the boiling point. The reagent for use is made by mixing 10 to 15 drops of the benzidin solution with 2 or 3 cc. of a 3 per cent. solution of hydrogen peroxide. A few drops of the feces mixture are added to this, and in the presence of blood a green or blue color appears in one or two minutes. If much blood be present, the blue color predominates.

Einhorn has simplified the test by preparing a benzidin paper, made by moistening filter paper with a saturated solution of benzidin and glacial acetic acid and drying it. (One must avoid contact with the fingers, as a drop of perspiration causes a similar reaction.) His method is as follows: A piece of benzidin paper is immersed in the solution to be examined, and a few drops of hydrogen peroxide are added. The paper is placed on a white porcelain dish and examined for the development of the blue color. This appears in positive reactions within one minute, or in great dilutions after a somewhat longer interval. Certain precautions must be observed in Einhorn’s modification. Farina and boiled potato produce a reaction, so that in examination of the gastric contents the liquid parts alone must be used. Hydrochloric acid may likewise cause a reaction, but this is delayed beyond two minutes, so that one minute should be the maximal time limit for deciding upon a positive reaction. The paper method is recommended as a valuable preliminary test, which, if doubtful, must be confirmed by the aloin ether extract method. For examination of the stools, one takes a small piece of the feces, rubbing it up with 2 cc. of water, and immersing the benzidin paper. The hydrogen peroxide is then added and the color reaction observed. Certain limitations of this test must be noted: Some salts of iron, some organic fluids, *e. g.*, saliva and sweat, certain chlorophyll-containing vegetables if unboiled, all may give a positive reaction. The patient must, therefore, be dieted to some extent, preferably with lacto-farinaceous and egg foods. The action of the digestive juices will not prevent a reaction.

*The Value of Tests for Occult Blood.*—After satisfactory exclusion of all extraneous sources of the blood, a positive result suggests a lesion of the mucosa in the alimentary canal, and three tests in succession must be made. If the mouth and the rectum be excluded as a cause, the source of the lesion is more limited still. When no evidence of inflammatory disease exists, *e. g.*, enteritis, and where no general disease is found (*e. g.*, cardiac or hepatic), a positive test for occult blood suggests ulceration—benign or malignant. Repeated positive tests occur more usually in cancer; the persistence of negative findings strongly suggests the absence

of any malignant disease of the alimentary canal. The prognosis of ulcer depends to some degree, too, on the results of occult blood tests, for the recurrent presence means imperfect healing and therapy is governed accordingly.

**Signs.**—But little is to be gained from physical examination of the stomach in acute ulcer. Tenderness is a common finding and yet the clinician who attaches too much importance to it alone is liable to be surprised and disappointed at an exploratory laparotomy. The tender point is often localized in the epigastrium, sometimes more diffuse. In pyloric ulcer it is apt to be in the right hypochondrium, though no rule obtains. No tumor is palpable in fresh ulcer. In older ulcers which have become callous or when scarring has occurred and causes pyloric obstruction or deformities in the stomach, the objective signs may be much more marked. Peristaltic movements, perhaps a dilated stomach, may be seen on inspection, while palpation may reveal a tumor of varying size, more or less movable, according to its situation and the presence of adhesions, usually at some part of the upper abdomen. The palpable mass present is either from the thickened ulcer itself, from muscular hypertrophy or adhesions, or may be due to fibromatosis (A. Thompson).

**Gastric Analysis.**—This varies according to the type of the ulcer. In the acute forms the examination of gastric contents may show little that is abnormal. The hydrochloric acid may be normal in amount, the proteolytic digestion unimpaired, and the motor power good. At other times there may be hyperacidity with hypersecretion, or the reverse, and motor insufficiency may be evident. Blood is often present, and may be visible to the naked eye or found only by microscopic or chemical examination. In the more chronic forms the findings will depend on the site of the scarring ulcer. If pyloric stenosis is present, there is usually hypersecretion with retention of food, good digestion of proteins, and little or no change in the carbohydrates. Sarcinæ are usually found in such cases, and also yeast cells in abundance. Blood, too, either evident or occult, is common. Lactic acid is present only where there is stagnation and hypochlorhydria. Rutimeyer found motor insufficiency of the first or second degree in 42 per cent. of his cases.

**X-ray Examination.**—The use of the fluorescent screen and the subsequent skiagram forms a most useful adjunct to the diagnosis of ulcer. The routine method is best carried out by examination in the morning on an empty stomach, after purgation on the previous evening. The first examination is made after giving a "Barium sulphate porridge," first by the screen, and then a photograph is immediately taken. Six hours later a second examination is made for residue, and for noting the propulsion of food. A liquid bismuth solution is then given, and screen examinations made to watch the tone and contractions; palpation for mobility is also performed. A "bismuth pap" is next taken to fill the stomach to determine irregularities of outline, as also mobility and peristalsis, and a skiagram completes the examination.

The employment of the x-rays in the detection of acute fresh ulcer has no foundation as yet, and the presence of a small metallic shadow has not been shown to be pathognomonic of such cases. In *fresh* cases

the *x*-rays may show signs of functional disturbances, *i. e.*, spastic contractions which may or may not be associated with ulcers or perigastritis, or there may be evidences of altered motility, but these are not more than adjuncts. The coincidence of pressure points with the area of spastic contractions seen under the screen is equally dubious, but when perigastritis occurs from chronic ulcer the contraction may be marked, and the stomach may assume an hour-glass shape—temporarily or as a permanent condition. The persistent coincidence of painful point and irregularity of the viscus on the skiagram may confirm a suspicion already existing, as Bonniger has found.

When *chronic* ulcer exists, the *x*-rays shed much light, and in various ways—normal peristaltic waves may be interfered with, the lumen may be encroached upon, mobility and motility may be altered, and the functions of the pylorus disturbed. Ulcers usually induce *hypermotility* with inhibition of pyloric closure, *i. e.*, pyloric insufficiency with quicker emptying of the stomach; such is Rieder's view, although there is no doubt that many variations occur, owing to the size and other physical conditions of the ulcer. When duodenal ulcers occur, *hypermotility* is the rule (Baetjer and Friedenwald). It is, however, the more callous, crater-like ulcers, those which have penetrated into deeper structures, with perigastritis and deformities, that demonstrate the value of the skiagram for more accurate diagnosis.

Ever since this discovery the frequency of these penetrating ulcers has been repeatedly shown, and means of diagnosis between chronic ulcers and cancer have been afforded that were previously beyond our reach. Briefly, one sees the following general conditions: (1) A metal shadow in one spot from the presence of the intraventricular crater-like ulcer with thickened walls. (2) An abnormal spot of metal shadow, lying in a niche or pocket, (extraventricular), apart from the general picture, connected to it by a channel like a diverticulum lying toward the lesser curvature, or quite separated. This shadow remains long after the rest of the metal has passed on into the duodenum and lower, a bubble of gas lies over it, and palpation for mobility makes no appreciable impression on the metal. This picture is due to the crater-like pocket formed by the penetration of the thickened ulcer, and its extraventricular extension, nearly always from the lesser curvature. Further, the incisure or transverse contracture may be seen, indenting the greater curvature. A *residue* after six hours, delayed opening of pylorus, and rapid settling of the metal to the lowest level come from atony. Sometimes deformity exists from the scarring, a perigastritis, or a true hour-glass stomach. The *x*-rays in simple perigastritis show no isolated niche of metal and no air bubble.

With *hour-glass* stomach the *x*-rays show saccules of varying size and number, usually two only, connected by a channel, which in length, size, and contour, varies according to the lesion. The pyloric sac in these ulcer deformities is usually larger than the ulcer, and shows signs of food retention because of pyloric spasm. The upper or cardiac sac, on the other hand, is more distended in cancer, for the lower empties more quickly because the pylorus is usually insufficient, through fibrosis.



These views of course contradict the findings of older observers by use of the tube. The metal shadow shows the retraction on the greater curvature which is drawn up toward the lesser, so that the canal between the two sacs is always found at the lesser curvature. This is in contradistinction to the hour-glass contraction of cancer, which shows a median channel and a "minus" in the metal shadow, instead of a "plus" as in ulcer. In other words, in ulcer there is a plus shadow because of the defect, while in cancer the tumor does away with the metal shadow at the point of the growth. In ulcer, too, the outline of the connecting channel is smooth by comparison, its transition into the lesser sac being more sudden.

**Diagnosis.**—A careful consideration of all the signs and symptoms is essential, and the anamnesis is above all things important; no one symptom or test is pathognomonic, but pain, tenderness, vomiting, the presence of blood whether manifest or occult, continuous hypersecretion and pylorospasm are the more important signs, and are characterized by their periodicity and intermittency. In the more *acute cases* with hemorrhage, it is not usually possible to differentiate absolutely between simple round ulcer, hemorrhagic erosions, and the oozings from the mucosa which have no demonstrable anatomical lesion.

Pain and tenderness as signs of gastric ulcer are unreliable signs in themselves, and disappointments often come from the laparotomy performed on the basis of these signs alone. The gastric analysis, too, is never pathognomonic, indeed it usually leaves one as uncertain as before, even if showing hypersecretion. Some authorities regard the presence of much gas with hyperacidity as strongly suggestive of ulcer. Evidence of blood intimately mixed with the contents is likewise an adjunct to a positive diagnosis. The x-rays furnish no aid in the diagnosis of acute ulcers. The seat of the ulcer is not readily determined, unless at the cardia when pain occurs with deglutition, or sometimes at the pylorus or in the duodenum, when with other signs the pain occurs several hours after the ingestion of food. Many exceptions, however, could be recorded.

Einhorn has invented a duodenal bucket, and Bassler a somewhat similar "string" test, the object in each case being to detect the presence of an ulcer and possibly its location by means of the blood stain, or brown-black discoloration on the string, from contact with the eroded surface of the ulcer. The bucket or shoe button, or B. B. shot with string (No. 8 braided silk) attached and of known length, is swallowed on the evening and is removed in the early morning and examined for any stain on the string. The situation of the stain on the string, measured according to its distance from the incisor teeth, determines the site of the lesion.

In the more *chronic cases* diagnosis depends especially on the anamnesis and physical signs, and much assistance is often gained through the use of the fluorescent screen and the skiagram. The history of pain, more or less intermittent, localized, and accompanied by tenderness, the recurrence of vomiting, sometimes with blood, the absence of marked and progressive emaciation, the frequent hypersecretion, all point to ulcer. Sometimes with these signs the scarred ulcer is palpable as a tumor.

**Differential Diagnosis.**—One must differentiate between ulcer and many other conditions, among which may be mentioned gastralgia, hyperesthesia, hysteria and simple hypersecretion, pylorospasm, gastritis, cancer, cholecystitis and cholelithiasis, renal calculus, pancreatitis, aneurism of the abdominal aorta, and even spinal disease and tabes with gastric crises. In most of these conditions the careful consideration of the anamnesis with the physical findings make clear the underlying disease. In some, however, the differentiation is not so easy.

*Hypersecretion.*—Simple hypersecretion (gastrosuccorrhœa). In this condition, which in its pure state is a functional disorder of secretion, there is absence of the positive signs of ulcer (vomiting, tenderness, hemorrhage). The pain is digestive in time, the analysis shows HCl in excess, and proper treatment directed against the secretory trouble is effectual. When the correct therapy fails, an ulcer, or other irritation, should be suspected as the cause of the trouble.

*Gastralgia.*—In this there is paroxysmal pain, not directly excited by food, nor related to or regularly affected by its ingestion. Pressure often relieves the pain; there are no tender points. If there be vomiting (and usually this is inconstant and irregular in onset), it does not necessarily give relief to the pain. Digestion itself is normal, and milk or other bland diets are of little use in the treatment. Aerophagia and eructations of gas are common. Neurasthenic symptoms and mucous colitis are often superadded. Epigastric pulsation is common. Hematemesis is absent, as also occult blood. Gastralgia often accompanies *uremic* symptoms, but there are other signs present, and the urine will probably be characteristic.

*Gastritis.*—A cause is present; the pain is more diffuse, less severe, and not increased much on pressure. The tongue is foul and coated. The vomitus contains much mucus, often organic acids, and there is usually diminution in the amount of free hydrochloric acid. If blood be present it is rarely large in quantity. Certain cases of gastritis with hemorrhage are at times indistinguishable from ulcer.

*Cancer.*—Debility and emaciation often precede the other signs; the pain is more constant and more independent of food, is often nocturnal, though it may at times be quite absent, and there may be simply a discomfort. The breath is foul and there is anorexia, as a rule; vomiting, which is common, gives less relief than in ulcer. The vomitus is rather that of motor insufficiency, and shows little or no hydrochloric acid, but usually some lactic acid, and other evidences of fermentation in the odor and in the presence of ill-digested food and the Boas-Oppler bacilli. Any hematemesis that occurs is more of the character of coffee-ground vomitus. Occult bleedings are more constantly found than in ulcer. The case is somewhat different where ulcer exists as a pyloric tumor with dilatation of the stomach, or where a cancerous growth has been engrafted upon a previous ulcer. Cancer limited to the pylorus is rare; the onset is obstructive, with vomiting, cramps, and emaciation, in a more elderly person; the course is progressive, and dietetic treatment affords no relief. If first seen when dilatation is really pronounced, the diagnosis must be made chiefly from the history and by examination of the gastric

contents and stools. Free hydrochloric acid is absent in 90 per cent. of these cases and lactic acid is evident. With ulcer there is usually hyperchlorhydria, or a normal amount of hydrochloric acid. The history of ulcer causing dilatation is of years' duration, because the condition is one of gradual development. The appetite improves with lavage, as also does the general condition. Where there is a cancer engrafted upon an old ulcer, there is increase in the pain, especially if there be some emaciation and weakness; the hydrochloric acid is gradually lessened; and the tumor increasing in size assumes a more nodular character. The skiagram is of great assistance.

**Gallstones.**—The differential diagnosis is often extremely difficult, and in a number of cases quite impossible for the time being. This is especially the case when the ulcer lies at the pylorus or is in the duodenum. There may be persistent pain, as in ulcer, especially after the taking of food, and with it vomiting; the vomiting may give relief; there may be tender points, and upon careful treatment even the symptoms may for the time disappear, and all this without jaundice, bile in the urine, or other signs of gallstones. As a rule, however, there is sudden, colicky pain at any time, of great severity and subsiding suddenly, tenderness in the right hypochondrium, slight fever, and perhaps sweating. Retching and vomiting occur with the pain and give no relief, pain continuing long after the stomach is empty. There are intervals of health and normal digestion. The co-existing gastralgia may be paroxysmal, and there is often hyperacidity. Not infrequently the sclerotics are subicteroid, and a trace of bile may be found in the urine.

**Complications and Sequelæ.**—The most important are: perforative peritonitis, perigastritis (suppurative and adhesive), subphrenic abscess, fistula between the stomach and adjacent organs, abscess of the liver, chronic hepatitis, acute and chronic pancreatitis, constriction of the bile-duct with jaundice, cardiac stenosis, pyloric stenosis, deformities of the stomach with dilatation or hour-glass stomach, cancer of the stomach, general emphysema, parotitis (sometimes with perforation and sometimes after hemorrhage), tetany, hemorrhage, anemia, etc.

**Perigastritis.**—As a result of chronic ulcer, peritoneal reaction occurs in the vicinity, and may be infectious in origin. The resulting inflammation may be suppurative or merely adhesive. Adhesions occur to neighboring organs or to the parietal peritoneum, and symptoms are thus produced which may give a clue to the diagnosis of the complicating condition. Surgical experience indicates that these are extremely common. The adhesions form most commonly about the lesser curvature, in the mid-region in front and behind, where the parts, too, are most at rest; also at the extreme ends of the organ, cardia and pylorus, described by the French writers as precardiac and prepyloric perigastritis. They are firm, well organized, and thick, and extend well beyond the limits of the ulcer and in extreme conditions even to the pelvis. With pyloric ulcers the gall-bladder and liver may be firmly bound to the stomach and gastrectasis thus commonly ensues. Sometimes an hour-glass stomach is formed often with penetrating ulcers. The *x*-rays have shed much light on these cases. The ulcer very frequently penetrates



deep into the adherent parts, forming tracts with expansion at the end, in which the bismuth shade is constant for days following the meal.

*The Symptoms.*—The location and degree of adhesions, as well as the type of inflammation, determine the course and special symptoms. The special features are pain, tenderness, and chronicity, without either cure or markedly progressive failure of health. Gallstones, angio-cholecystitis or cancer, may simulate the condition or a secondary pyloric stenosis, or the perigastritis may be a mere accompaniment of a neighboring disease. Signs of ulcer have usually been present for a long time previously, and to these are added exacerbations of the *gastralgic pains* often radiating to the back or upward, only to some extent relieved by rest, and increased on forcible straightening of the trunk. Ingestion of food or fasting has no lasting effect on the symptoms. Examination reveals perhaps nothing but tenderness, or there may be increased resistance and even a definite mass, which is subcostal, perhaps superficial.

The differential points are briefly: A previous ulcer or one still unhealed, with a history of long standing and yet an absence of cachexia and metastases; perhaps gastrectasis; persistent pains more or less influenced by posture and sudden exertion; localized tenderness; occasional jaundice without involvement of the liver; periodical febrile attacks of short duration. Gastric analysis gives no distinctive results. The *x*-rays are of great value here, revealing frequently a perforating ulcer with fixation of the viscus from perigastric inflammation.

**Perforation.**—This is one of the most serious complications of gastric ulcer, and occurs in a varying percentage of cases (1 per cent., Leube to 18 per cent., English). Clinically, in 1336 cases there were 45 perforations, *i. e.*, 3.4 per cent. In 1615 autopsy cases there were 336 perforations, *i. e.*, 22 per cent. *General peritonitis* occurs chiefly when the perforation takes place rapidly before adhesions form. The extent depends upon the time from onset, for the transverse colon and the mesocolon act as temporary barriers for a few hours before extension occurs into the lower half of the peritoneal cavity (Berg). Perforation of a gastric ulcer sets up a general peritonitis more commonly than does a duodenal ulcer, perhaps because the duodenal contents are more sterile, or because there are more chances of adhesions. The same rule applies to pyloric ulcers as compared with ulcers elsewhere in the stomach.

*Course of Perforated Ulcer.*—Sometimes, though rarely, an acute perforative general peritonitis may heal spontaneously. This is extremely rare in the acute cases. Some subacute and chronic cases recover, although usually with conditions which lead to more or less chronic invalidism. *Extension* may occur in almost any direction. Perforation into the liver or pancreas may occur with abscess or chronic inflammation in either organ. There may be obstructive jaundice with pressure on or stricture of the ducts and a *catarrhal cholangitis*. Subphrenic abscess may occur, and was due to ulcer in 20 per cent. of 179 cases (Maydl). The *portal vein* is sometimes invaded, and *pylephlebitis* follows. The gall-bladder may be involved and stones may fall into the stomach through the fistulous opening. Sometimes the *spleen* is involved, and we may find a *perisplenitis*. If the perforation penetrates the *intestines*,

there may be a severe diarrhœa and bloody or purulent feces or fecal vomiting. A gastro-colic fistula may form; Murchison found 10 cases of this in 33 perforations due to ulcer.

Rarely perforation occurs into the *abdominal wall* with an external fistula. In the more chronic cases sometimes the perforation occurs at a place far distant from the original ulcer, by dissecting and pointing, as in one instance in which a pelvic abscess formed and was drained through the vagina some weeks after the perforation of the ulcer.

*The Symptoms and Signs of Perforation.*—The early signs are the most characteristic, hence the importance of seeing cases early, but there are no pathognomonic symptoms previous to perforation. The onset is usually sudden; indeed, the sudden pain or other distress may be the only sign of the ulcer, though a careful anamnesis is of the greatest importance in the diagnosis. English found no history of stomach trouble for some time before perforation in 11 of 50 perforation cases. The patient need not be overcome and incapacitated at once; sometimes he is able to walk into the hospital with such a perforation. In one case under Seymour Taylor's charge there was a single bloody stool as the only sign of perforation, without pain or abdominal signs of any kind, and a fatal result ensued with no other local development. It commonly follows some strain, such as vomiting, trauma, or a hearty meal.

*Pain* is the earliest symptom, is not only sudden but of great severity, usually referred to the epigastrium and spreading soon to the right and left, but not leaving its original site. Dyspnœa soon follows, and deep breathing causes pain about the diaphragm, so that these cases are sometimes mistaken for acute pleurisy. Vomiting is not so infrequent as was formerly thought, a small opening does not allow escape of so much contents—though with the gradually developing peritonitis, the cessation of a previously existing vomiting is very suggestive of perforation. Collapse and prostration supervene. In some cases remarkably little prostration is observed, a fact which is apt to mislead, especially as the general signs may greatly improve after a few hours before graver symptoms develop. The degree of collapse depends in large measure on the amount and extent of the extravasation. The face is anxious, often pinched, and there is apt to be great restlessness. The pulse is usually accelerated, though sometimes it is normal, and the temperature may be but little altered immediately after perforation has occurred. Usually there is slight fever.

The abdomen may be flat and tense, sometimes it is distended; the muscles are rigid, often in the upper zone only, and there is diminished mobility, two signs of greatest significance. Tenderness is chiefly about the epigastrium and hypochondrium. Eighteen out of a series of 49 cases were diagnosed as appendicitis. Percussion may or may not give dulness here, and the liver dulness need not be obliterated, although this depends in great measure on the escape of gas into the surrounding parts. The sign of obliteration of the liver dulness is unreliable. Even when absence of liver dulness exists as far back as the midaxillary line, it may imply no abnormality. Nor, again, is it true that well-marked stomach tympany in the left hypochondrium excludes the possibility

of perforation. A valvular perforative opening may exist allowing distension. On auscultation, a friction rub may be heard over the diaphragm, and sometimes the gurgling of fluid through the perforation.

*Pseudo-perforation* is not uncommon, *i. e.*, the signs and symptoms of perforation without other anatomical lesion than mere ulcer, as in a case recorded by Manges, in which a woman, aged twenty-seven years, after previous signs of ulcer (hematemesis, etc.), suddenly had pain and tenderness in the epigastrium, with a temperature of 102°, pulse 120 to 140, and marked rigidity. Operation was performed, but no perforation and no peritonitis were found, simply the uncomplicated gastric ulcer. Leukocytosis varies in this as it does in the perforation following typhoid fever. We are told that attention should be paid to the base of the thorax on the left side, where one often obtains restricted movement, localized pain, and tenderness, with dulness in the lower axillary region and other signs of fluid (Osler). Fluid may collect beneath the diaphragm about the anterior and external surface of the spleen, or in the lesser peritoneum, and later on the usual signs of general peritonitis may develop.

**Cancer Developing upon Ulcer.**—Cruveilhier first suggested this possibility in 1835, although he believed a cancerous diathesis essential to its development, and Rokitsky, in 1839, added further observations on its probable concurrence. The importance of ulcer as a possible cause of cancer has since then been repeatedly suggested and perhaps much exaggerated (Wilson and MacCarty, 71 per cent.), for pathologists incline rather to the opinion that where the two conditions co-exist, the ulcer is a secondary degeneration of the cancer and not *vice versa*. Such is Aschoff's view.

Any dogmatic statement on the origin of cancer from ulcer seems impossible in the present state of our knowledge, and other methods of deciding this dubious point must be looked for. Clinical histories seem to point to the possibility in some instances and a definite anamnesis applicable to such a transition exists. It must be admitted, however, that a history of gastric trouble prior to cancer does not mean a pre-existent ulcer, and that, on the other hand, many cancers may grow slowly over a period of years before declaring themselves, and thus perhaps the so-called transition period was one in which cancer alone was present from the start, though without showing clinical or pathological evidence. Paterson has pointed out the infrequency of duodenal cancer in spite of the ever increasing records of ulcer in that location, and that ulcers left alone after short circuiting rarely show cancerous change. Friedenwald's statistics likewise show but a small proportion of cancers arising from gastric ulcer (7 per cent.).

*The Symptoms and Diagnosis of Cancer Forming on a Previous Ulcer.*—The transition period between the signs of the original ulcer and the onset of the cancer varies greatly. There are some undoubted cases on record, and the duration of symptoms in these has varied; it is sometimes short, or, in others, years have elapsed since the ulcer first formed. Malignant development is suspected when loss of weight persists with a cachexia greater than a mere ulcer would justify. In such cases, too, there is



more constant pain, although perhaps even less intense, and its character alters to a more dull, sickening ache. Tenderness is more diffuse. There is more nausea and vomiting; at all events, the vomiting is more regular, and even if a longer time intervenes between the attacks, it is more copious and rancid, and readily excited by liquid food. Blood appears more frequently in the vomitus, and in small amounts; and occult blood is more constant in the feces. The appetite usually becomes less, the patient is more languid, nervous, and weak, and is markedly anemic. The gastric analysis is not always characteristic of cancer and then only late in the disease, and often hyperacidity is present to the end. Mechanical and medical treatment are without avail, and if, with proper ulcer treatment, there is increase of the symptoms, especially emaciation, pain, vomiting, anemia, and weakness, cancer may be suspected.

**Parotitis.**—This is not common. S. Paget and Hone mentioned several cases in 1897, and English reported 5 instances among 50 cases with bilateral parotitis. Sometimes suppuration occurs. The condition probably arises in the same manner as in other diseases of the abdominal and pelvic viscera. Rolleston and others, while dubious as to its causation, do not regard the complication as arising from infection of Stenson's duct.

**Tetany.**—This, while commonly associated with old scarred ulcers with dilatation, sometimes occurs without any such complication. Moynihan had 5 cases. There are mild and severe grades, the former with mere cramps and paresthesias at times, the more severe forms often resulting fatally. Albu reported 31 deaths out of 40 cases. Any source of irritation may induce an attack, and not infrequently the mere lavage of the stomach which so often relieves the symptoms may at other times precipitate an attack. The tetany is supposed to arise from some auto-intoxication due to absorption of decomposed gastric contents.

**Pyloric Stenosis with Dilatation.**—(See article on Gastrectasis and Motor Insufficiency.) Dilatation is fairly common and is associated either with pyloric stenosis from a scarred ulcer or perigastric adhesions as direct causes, or with contraction or spasm of the pylorus and mechanical irritation as indirect causes.

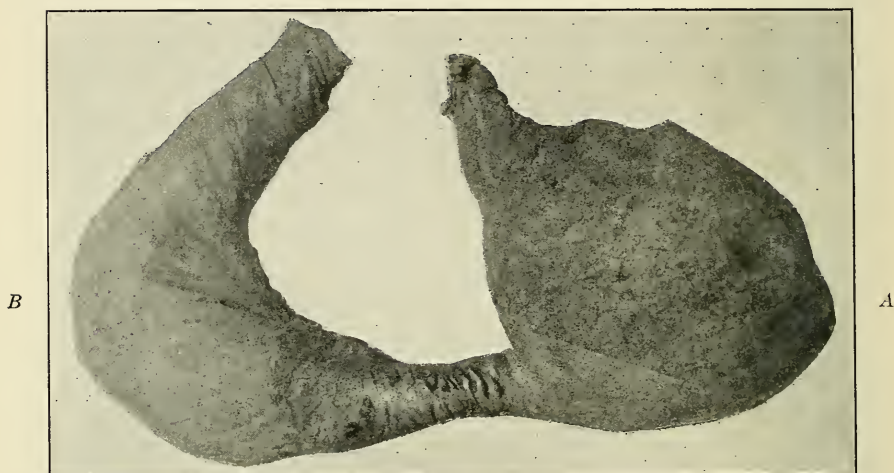
**Cardiac Stenosis.**—This may occur from cicatrized ulcers at the cardiac end of the stomach as also diverticula at various portions from similar causes, or through traction of perigastric adhesions.

**Hour-glass Contraction of the Stomach.**—*Sanduhrmagen, l'Estomac Biloculaire.*—This condition is much commoner than was supposed formerly, largely owing to the findings in surgery and by the *x*-rays. It consists of a contraction anywhere between the cardia and the pylorus dividing the stomach into two or more portions; sometimes it is trilobular. Moynihan has described a case with four sacs.

**Etiology.**—The condition is rarely a congenital one. Moynihan denies any such origin and deals with individual instances, which he claims as being inaccurately described as congenital, regarding it as almost always dependent on some organic disease from one of three causes—ulcer, perigastric adhesions, or carcinoma. Nevertheless, in one of the speci-

mens in the McGill Museum removed from an infant, the condition is so marked, as to leave no other conclusion than that it was, at all events in that instance, congenital. Meckel has the same view of its possible origin. The direct and most common cause is an old ulcer with cicatrix or adhesions of the stomach wall or other parts, or both, or the formation of independent bands of fibrous tissue. Among 48 cases reported by Robson and Moynihan in 1906, 41 were due to ulcer. Other cases are not infrequently associated with cancer of the stomach, while tuberculous peritonitis may cause bands of fibrous tissue to form about the stomach and produce identical results.

FIG. 3

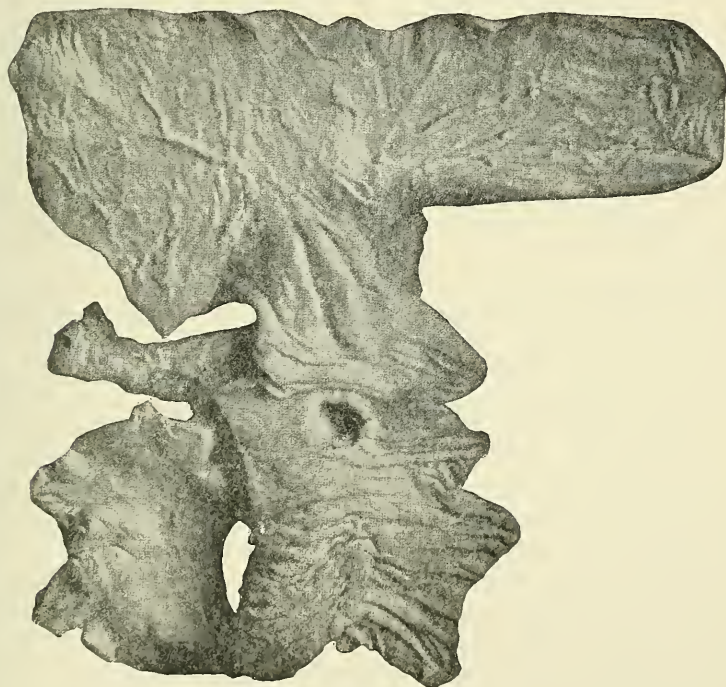


Hour-glass contraction of the stomach: A, cardiac portion; B, pyloric portion.

The *symptoms* are at times quite indefinite, and at other times appear to be quite characteristic. They apparently depend on the original cause at first, but later the effect may be diagnosed, provided one exercises sufficient care and patience. As has been pointed out by others, the main symptoms are pain after meals, vomiting of stomach contents and sometimes also of blood, emaciation, and the presence of a tumor, due to cicatrization of old ulcers, with an absence of secondary nodes and of ascites. The condition is naturally associated with symptoms for many years, and the patients suffer much. For a time the symptoms seem to simulate stenosis of the pylorus, the presence of pathognomonic features depending largely on the site of the contraction. This, as a rule, lies four inches from the pylorus, and therefore simulates pyloric obstruction with dilatation, all the more so as hyperacidity usually co-exists and the *secondary cavity* is small. Moynihan gives the following sets of symptoms, the result of the experience of various authors: *First*, in lavage of the stomach, all the fluid fails to return, some, which is in the secondary pouch, being apparently lost (Woelfer's first sign); *second*, after lavage has apparently thoroughly cleaned the stomach, more

contents reappear, probably foul and evil-smelling, the washings thus being again dirty (Woelfer's second sign), or the same may be found on withdrawing the tube after washing the stomach clean and then passing it again; *third*, the sign of paradoxical dilatation (Jaworski); this consists in the succussion splash on palpation after apparent removal of all the gastric contents, a sign which is of course present because only the cardiac sac is emptied; *fourth*, after percussing out the stomach and then distending it, a change in the position of the distension tumor is found at times. First the proximal pouch is distended and then the distal, and the notch is often visible between the two tumors when both parts are dilated (von Eiselsberg); bubbling and sizzling are distinguished at a point distinct from the pylorus on dilatation (von Eiselsberg), and patients are sometimes themselves conscious of this and of food passing from one pouch to the other. This may be detected by the stethoscope. The *x*-rays form by far the most satisfactory means of diagnosis.

FIG. 4



Duodenal ulcer.

**Duodenal Ulcer.**—Many ulcers diagnosed as duodenal prove to be pyloric and *vice versa*. Duodenal ulcers are very common, and surgeons have proved that their frequency approaches that of gastric ulcer. They are commonest in the third decade, though no age is exempt, and perhaps oftener in males. Tull found equal numbers in males and females in the Montreal statistics. As to the *site*, 90 per cent. or more



occur in the first portion, while they are least common in the lower portions. Practically all those in the first portion extend to within three-quarters of an inch of the pyloric sphincter, and the deepest portion is usually just below the pylorus, where the acid chyme most affects the intestinal mucous membrane. In 6 out of 10 cases in MacCallum's series the ulcer was on the posterior wall; in the other 4 it was situated anteriorly.

**Number.**—Collin found one ulcer alone in 80 per cent., two ulcers in 11 per cent., three to four ulcers in 4 per cent. When multiple they are usually crowded together in the first portion. Moynihan, in 1902, drew attention to the co-existence of gastric and duodenal ulcers.

**Symptoms.**—While, as in gastric ulcer, many cases run a latent course (91 out of 151 of Perry and Shaw's cases), yet, as a rule, pain is the prominent symptom, and is present in 80 per cent. of all cases. In some cases the pain resembles severe biliary colic, for which, indeed, it is often mistaken, especially if, as commonly happens, jaundice is also present. Long intermissions with recurrent pain extending over months or years are not uncommon. Radiation of the pain is by no means the rule. It is usually local only, although at times it radiates to the breast, shoulder, or back. While usually related to the ingestion of food, in that it comes on from one to four hours after, it is not necessarily so. It is at times relieved by food, drink, lavage, or alkalis. The pain may be associated with local peritonitis, spasm, the action of acids, or, again, with gaseous distension. *Tenderness*, if present, is perhaps more frequently to the right of the median line, although quite often only in the epigastrium. It is at times diffused and not localized. It is rarely posterior.

*Vomiting* is less common than pain, being present in less than 20 per cent. of the cases. It is irregular, delayed, often acid, and the amount varies according to the amount of obstruction and of hypersecretion. *Acidity* is usually increased, and hyperchlorhydria has been frequently found. The appetite remains good and constipation is the rule. *Hemorrhage* from the stomach or bowels is common. Oppenheimer found melena in 50 per cent. The diagnosis is made more commonly from the association of the local tenderness and the melena, or even from the tarry stools in the absence of pain than from any other signs. Sometimes hematemesis and melena occur together, and there may be so much hemorrhage as to produce a fatal result. It is severe in at least one-third of the cases. The hemorrhage of duodenal ulcers is more difficult to check and usually of longer duration than that of gastric ulcer. In the 23 pure duodenal ulcers recorded by Moynihan, 4 had both hematemesis and melena, 3 had hematemesis alone, and 4 had only melena.

Loss of weight is common, and is probably often due to insufficient nourishment being taken, from fear of pain after ingestion of food.

The *clinical types* of duodenal ulcer may be divided into: (1) Those indistinguishable from gastric ulcer in symptoms and signs. (2) Those with hemorrhages from the stomach or bowel, or both, and with no other symptoms. (3) Those with symptoms resembling biliary colic, especially

the pain, tenderness, and intermittent jaundice. (4) The perforative cases, which simulate gall-bladder perforation and appendicitis.

**Complications.**—These are numerous, and the most notable are: Perforation, periduodenitis, implication of the gall-bladder and bile-ducts or of the pancreas, cicatricial stenosis of the duodenum and ampulla of Vater, with obstruction of the outflow of bile and pancreatic juice, compression of the portal vein, and cancer. *Perforation* occurs frequently, (43 per cent., Chvostek). Of 131 collected cases with perforation, 91 per cent. were in the first part, 6 per cent. in the second part, and 3 per cent. in the third portion; 80 per cent. were in males. Nearly all perforations are anterior (in 20 per cent. there are no preceding symptoms of ulcer).

**Diagnosis.**—Wrong diagnoses are frequently made, and many cases with perforation have been mistaken for appendicitis (19 out of 51, Moynihan). The mortality of perforation cases, while 80 per cent. in Brunner's time, is now much less, and modern methods of diagnosis and clean surgery have done much to improve statistics of cure. Early operation is most important and delay beyond twenty-four hours adds greatly to the risk.

**Course and Prognosis of Gastric Ulcer.**—The fact that so many gastric ulcers are latent, and the difficulty attending the diagnosis of simple cases has made it impossible to determine with accuracy the average duration. Many cases, if not the majority, are undoubtedly acute in onset, and while some heal rapidly within a few weeks or less, others are of many years' duration. In MacCallum's and Tull's cases, some had a history of ten or more years, with intermissions, while some duodenal cases gave symptoms for twenty years. It is difficult to say, however, how much of the history was attributable to ulcer, and in how many cases multiple ulcers occurring at long intervals may have given rise to the prolonged symptoms.

The mortality from all kinds of ulcers is variously given as 8 to 10 per cent. (Riegel). Russel, in England, has investigated the after-histories of cases of hemorrhage, and finds the direct mortality 2.1 per cent.; 4.3 per cent. died of intercurrent diseases; 42.6 per cent. recovered (27.7 per cent. had only one attack, and 14.9 per cent. recovered after one or more relapses); 6.4 per cent. were indefinite as to the prognosis and 44.7 per cent. still had gastric symptoms of varying intensity. Leube claims 50 to 75 per cent. of cures after four to five weeks of medical treatment, and holds that when cases are thereafter refractory, no medical treatment is of any avail, and surgical interference is justifiable. Lenhartz's results would seem to give even a more favorable outlook, and modern surgery, with its excellent cures through timely gastro-enterostomy, has entirely altered the former unfavorable statistics. Relapses are frequent, and may occur after several years. Einhorn's views are most encouraging as regards the prognosis of gastric ulcer. He draws attention to the fact that at postmortems one sees twice as many scars as fresh ulcers. Older ulcers are in some respects more favorable. Sometimes a new ulcer forms alongside of an old and chronic one, and again sometimes cancer forms on the ulcer and quite alters the complexion of the case and the outlook.

How can we determine if an ulcer is healed or not? This is fraught with difficulties. In general, one may say that if the patients are free from digestive complaints, if pain is absent, especially after solid food, if epigastric tenderness has disappeared, and if no occult blood is found in the feces after repeated tests, the conclusion is reasonable that healing has occurred. This idea is strengthened by the additional evidence of normal weight and strength. Postmortem, however, one sometimes finds open ulcers which have given no symptoms for several years, showing that in spite of latency of all symptoms, healing may not be complete, or recurrence may have taken place.

**Treatment.—Prophylaxis.**—The etiology of gastric ulcer being still obscure, it is not easy to suggest along what lines the occurrence of ulcer may be prevented. We may say, maintain good health and a normal nervous system, and protect the stomach against irritation.

Early diagnosis is of paramount importance, not only to prevent complications later on, but to effect a cure. The acute and the chronic ulcers require different treatment, according to their physical conditions. For the cases of so-called *acute* gastric ulcer, the strictest discipline is essential to a cure, and no neglect in hygiene, diet, or medicine is permissible. Failures in medical treatment come from indifference or incomplete discipline. The essentials of treatment are: (1) Protection of the mucous membrane. (2) To counteract hypersecretion. (3) To counteract causes of hypersecretion (irritation). (4) If operation is performed, continue the same care. *Rest* in bed is essential once the diagnosis has been established and the treatment commenced. By resting from at least four to six weeks in this way, hemorrhage and perforation may be prevented, and less of caloric units are required in the diet. After this the transition from rest in bed to walking should be very gradual, and when once able to go about the patient should be made to rest after every meal. These precautions should be observed for some months or even longer; sometimes even this does not suffice.

**Diet.**—There is no general rule of feeding applicable to all ulcer cases. Each patient must be considered individually; some may require more, others less food; when the motor power is good and the stomach not readily contracted through spasms, a more generous diet may be recommended. If, on the other hand, the stomach is irritable and food causes pain and distress, it is well to give such patients as little food as possible and proceed very carefully in the transition to a more liberal diet.

In the so-called *abstinence cure*, during the first few days one depends exclusively upon rectal alimentation. This gives complete rest to the stomach, and may if necessary be kept up for several days, provided some nutrition be maintained per rectum. Saline enemata alone may suffice, but starvation is good, and often well borne.

Saline injections are specially commendable because less gastric secretion is produced than when nutrient enemata are employed. One may, however, if preferred, give nutrient enemata, the patient receiving every six hours six ounces of broth with an egg and salt, and if desirable a little whisky may be added. These enemata should be given by means of the funnel and tube, slowly and by gravitation, and the bowels should



be gently irrigated before every second or third enema. Ewald recommends an enema made up of two or three eggs beaten up with one-half ounce of cold water, this mixture being added slowly to another made up of a few starch granules boiled in one-half cup of 20 per cent. grape sugar, to which two ounces of claret are added when lukewarm, the total being eight ounces. This should be introduced slowly high up, and should, if there be a previous cleansing saline injection, cause no irritation. This may be used twice or three times daily for from three to eight days. Water enemata may be used at intervals between the nutrient enemata if there is thirst, a dry tongue, or a bad breath.

**Mouth Feeding.**—The early administration of food by the mouth is apt to cause distension, increase the hyperacidity, induce vomiting, and thus directly or indirectly prevent the healing of the ulcer. When food is administered by the mouth it is well to commence with milk and lime-water, albumin-water, or strained oatmeal gruel, at first in small quantities, a few ounces every two hours, and combine this as required with nutrient enemata. Whey is recommended by some. Milk may be given warm and diluted with one-eighth of lime-water or sodium bicarbonate. If curds form, one may add a little meal or flour to the milk, or peptonize it. To many butter is tasteful in the early stages of treatment. Fütterer strongly recommends the early use of beef juice. After several days of this diet one may add rice or sage soups, broths in small quantities, and raw or soft-boiled eggs, and at the end of two weeks finely divided albuminous foods, such as minced meat, white fish, chicken, partridge, and tender beef, and mashed potatoes. One cannot lay too great stress upon the necessity of care in the *transition stages* from the liquid to the semisolid diet. After six weeks other meats may be given, and from that time on the greatest care should be taken for several months, even after an apparent cure has been obtained, and all coarse, irritating, and spicy, rich foods should be avoided. Examination of the feces for occult blood is an excellent guide for change in diet.

**Medicinal Treatment.**—Perhaps the most universally employed drug in gastric ulcer is bismuth, which may be given as the subnitrate, or preferably the subgallate, in doses of from 20 to 30 grains (gm. 1.3 to 2) or more several times daily. It is perhaps best suspended in gruel or barley-water. It may be given alone or combined with sodium bicarbonate or calcined magnesia, which ease the pain and burning and counteract the hyperacidity. Bismuth, however, constipates, and may in this way be a source of trouble. The constipation may be relieved by Carlsbad salts, given in doses of one dram in hot water in the early morning; or it may be better at first to give merely enemata of soapsuds or glycerin. Fleiner's bismuth cure consists of daily lavage and subsequent administration through the tube of six ounces of water with  $2\frac{1}{2}$  to 5 drams of subnitrate of bismuth. The patient lies down for half an hour and then takes breakfast, this procedure being carried on for two weeks. It is very doubtful if the results and requirements justify a method of treatment so troublesome to the patient.

Silver nitrate is also highly recommended as an astringent and antacid. It may be given in pill form,  $\frac{1}{4}$  to  $\frac{1}{2}$  grain (gm. 0.016 to 0.03) per dose,

or in solution with a few grains of sodium bicarbonate. Some prefer giving it through the stomach tube. Boas uses silver nitrate in a solution of 1 to 500, and gives it in gradually increasing strength up to 1 to 300, adding peppermint to prevent nausea.

*Lavage* is carried out when the stomach is intractable; and for ambulatory cases some sodium bicarbonate may be added to the water.

**Treatment of Symptoms.**—For the *pain*, if severe, morphine may be necessary; a wet compress over the epigastrium is often soothing; orthoform may be used with some benefit. For the *vomiting*, ice, bismuth, nitrate of silver, cocaine, and opium are recommended. For the *anemia*, albuminate of iron may be given, as Ewald suggests, by adding 1 dram (4 cc.) of a 2 per cent. solution of iron sesquichloride to 2 ounces of albumin water; or Blaud's pills with a laxative may be used. For the *hematemesis*, absolute rest and quiet, ice to suck, and small doses of adrenalin chloride, 10 to 20 drops of the 1 to 1000 solution three or four times a day, may be effective. Lucas Championnière seems to have shown that lavage is good because the stomach is not in repose during hemorrhage, and washing out gives it the necessary rest. Ewald used ice-water for the lavage, and others recommend gelatin water. It is thought by some that high enemata of hot water, acting reflexly, may check the hemorrhage and combat the shock. It is well, perhaps, both for the restlessness and for the quieting of the circulation, to use morphine hypodermically. For the severe recurrent hemorrhages surgical intervention may be necessary, and is often most successful.

*Leube's Method.*—The patient is placed in bed for ten days, the epigastrium washed with alcohol and sublimate solution, then boracic ointment is applied on a cloth, and over this a hot flaxseed poultice, 20 by 10 cm., every fifteen minutes, for ten hours during the day; at night a wet compress is applied. This treatment is carried on for ten days. Then a simple cold compress is applied at night during the next three weeks, while in the day an abdominal flannel binder is worn. During convalescence the patient rests for two hours after meals, not even doing sewing, etc. The only contra-indications for poultices are menstruation and recent hemorrhage (within three months). When recent hemorrhage has occurred, or when the stools show traces of blood, an ice-bag may be applied instead of the cold compresses. One pint of Carlsbad water is drunk slowly each morning for one month, and alkaline waters are taken during the day. Few drugs are used, unless bismuth or sodium bicarbonate. The *constipation* is treated by enemata of tepid water, by Carlsbad salts, or other salines.

*Lenhart's Method.*—Bismuth subnitrate, 30 grains (gm. 2) is given daily with careful limitation of fluids. Morphine is unnecessary. Sometimes silver nitrate is useful, and iron later on. Occasional glycerin enemata may be given after the first week. In the diet fresh eggs are the main article, given in increasing quantities each day, chiefly raw and beaten up. One to three eggs are given on the first day, and one added on each subsequent day, until eight are taken daily, and this number maintained. They may be given iced in teaspoonfuls, and later soft boiled. Sugar is added to the eggs on the third or fourth day, in gradually

increasing amount (30 to 50 gm.). Iced milk must be given in extremely small amounts, only increased with the greatest care to obviate unnecessary distension, which Lenhartz regards as the most serious of all ordinary events which may obviate the healing process. Eggs alone being insufficient, finely divided meat, preferably raw, or scraped beef, is given from the sixth day onward (at first 35 to 70 gm.). On the seventh day, soft-boiled rice is given, and on the eighth day, toast, softened rusks, or cereals, and 20 to 40 gm. of butter, and finely divided raw ham on the tenth. Strong broths are harmful on account of their extractives and spices, which tend to increase hyperacidity.

The treatment is begun at once, in order to bind the hydrochloric acid and prevent its evil effects on the recent thrombus. Absolute rest is maintained by this means better than by the abstinence cure, for even with an empty stomach some peristalsis takes place and is only likely to be increased by an excess of hydrochloric acid.

*Senator* adopts a middle course and argues that one should not distress the stomach by an excessive amount or weight of food, that a soothing diet is useful to prevent recurrence of the hemorrhage, that a diet which will counteract the hyperacidity is useful, and that the food administered should be easily digested and nutritious. To this end he believes that gluten, fat, and sugar fulfil all these requirements. For this purpose he recommends *lerin*, or its modification *glutin*, or one may use gelatin because of its hemostatic effect. Fat is useful because of its counteraction on the acids, and its soothing effects on the surface of the ulcer. He allows fresh butter and cream in small amounts, often, *e. g.*, 30 gm. of butter and 250 cc. of cream in twenty-four hours. If the butter is not well borne, it may be given iced in lumps to suck or swallow. Cream is given iced and beaten up. These quantities may be gradually increased if no hemorrhage occurs, and one may add milk, beaten up eggs, and meat, as recommended by *Lenhartz*. Gelatin should be stopped after a while because of its constipating effect, and in its place one may use jellies. Instead of butter, good oil may be given, either iced or as an emulsion (almond emulsion or almond milk).

*Rosenheim* likewise approves of gelatin, using it in 5 to 8 per cent. solution in citric acid, and avoids meat, preferring a lacto-vegetable diet.

*Chronic ulcers* which have failed to respond satisfactorily to medical treatment are in some cases benefited by surgical interference; others, again, do not admit of operation because of associated gastric and other abdominal conditions which render the operation unsuccessful and merely aggravate the already existing misery.

*Einhorn* has recently devised a method of feeding directly into the duodenum by means of a tube especially constructed for this purpose, and claims some success in suitable cases—with persistent bleeding and tendency to stasis. The method does not seem to have received general approval, though in theory much might be said in its favor.

**Surgical Considerations.**—Many statistics have been compiled with a view to demonstrate the superiority of medical over surgical methods of treatment, and *vice versa*. Such proofs, however, scarcely carry



much weight when diagnoses are often uncertain, when conditions and symptoms vary within the widest of limits, and when the individual circumstances make it always imperative to consider each case by itself and for itself, rather than to place it under any very general category. Many cases certainly fail under medical treatment, and just what particular circumstances interfere with the healing of so many simple ulcers, even when seen in early stages, are as yet unknown. Certainly statistics now in use are for the most part unreliable and more or less useless.

Surgical interference shows an ever-diminishing mortality in each succeeding year since operations on the stomach have become common. While in earlier years operations were frequently repeated because of incomplete results, the number of these likewise attains an ever-diminishing proportion in accord with the more judicious selection of cases and better methods of operation. Repetition of operation was necessitated either from recurrence of old ulcers, from formation of new ones near the site of operation, persistence of old symptoms, the development of vicious circles, or hernia, but the proportion of these has rapidly lessened.

The following figures present the case as it now stands with modern surgery: Up to April, 1905, among 153 gastro-enterostomies, etc., (two only requiring second operation), there were 2 deaths (1.5 per cent.). Later, among 206 gastro-enterostomies, etc., including hemorrhagic cases and hour-glass stomach, there were 9 deaths (4.3 per cent.). In May, 1906, among 251 gastro-enterostomies, etc., there were 9 deaths (3.5 per cent.). Mayo Robson, among 210 gastro-enterostomies, etc., had 8 deaths (3.8 per cent.). Comparing these figures with those of earlier years, the improvement is striking, and comparing them with the mortality by medical treatment alone, the benefit attributable to surgery is enormous. Graham<sup>1</sup> reports from the Mayo Clinic that of 438 cases of duodenal ulcer which had been followed, 70 per cent. were cured, 27 per cent were improved, and 3 per cent unimproved. The results are slightly better when there is an obstruction present. This was even more marked in the gastric ulcers which caused obstruction. Of the patients with ulcer operated on during a period of six years, 76 per cent. were males and 24 per cent. females. In the males 70 per cent. of all ulcers were duodenal or involved the duodenum, and in the females 60 per cent.

Of 162 cases of gastric ulcer, 59 per cent. were cured, 22 per cent. were much improved, 13 per cent. showed some improvement, and 7 per cent. were unimproved.

**Surgical Methods and Indications.**—*Surgical Treatment of Perforation.*—Howard states that 8 cases have been recorded as recovering after generalized peritonitis without operation, and Carless' statistics, which seem optimistic, give 4 per cent. recovering under similar conditions. The early surgical treatment as a result of early diagnosis and perfected technique has given brilliant results, and the following statistics afford

<sup>1</sup> *Boston Med. and Surg. Jour.*, 1914, clxx, p. 221.

ample evidence of the success of more modern methods: Mikulicz, 1885 to 1893, had 35 cases with 34 deaths, *i. e.*, 1 recovery, and from 1894 to 1896, 68 cases with 36 deaths, *i. e.*, 32 recoveries. Tinker, in 1900, recorded 232 cases, with 113 recoveries, and Robson, in 1900, recorded 429 cases, with 279 recoveries (65 per cent.). J. Bell, of Montreal, in 1903, had 10 cases, with no deaths. The proportion of recoveries has a direct relation to the early time of operation after rupture; the sooner operation is done, the greater proportion of recoveries.

The multiplicity of ulcers is of the greatest importance, and is to be considered in all operations for perforation, and in not a few cases a second operation has been necessary for this reason, when the first had healed. Hence the recommendation of some surgeons to perform a gastro-enterostomy in all cases after closing the perforation, in this way obviating possible extension of other ulcers.

*Hour-glass Contraction.*—The treatment of hour-glass contraction is essentially operative, the object being first to drain both sacs and allow of healing, which, however, involves a double operation. Many methods are recommended. (1) Gastroplasty, which affords better communication between the two sacs, is a suitable operation for the simpler cases with little infiltration. It is done with or without gastro-enterostomy, according to the requirements. (2) Gastro-gastrostomy, in which the two sacs are brought together and directly joined, is often commendable in patients whose hour-glass contraction is extreme, and where the opening between the sacs is very small. (3) Partial gastrectomy, which removes the total area of disease and unites the divided healthy ends of the stomach, is the ideal operation, because it corrects the deformity as well as eliminates all the old or any recent disease. (4) Gastro-enterostomy alone is of little use. To be beneficial it should be double, and this makes a serious operation and affords some danger of a double vicious circle. The necessity for anastomosis is largely determined by the situation of the ulcer, its extent, and its liability to induce stenosis, adhesions, and deformities.

## CANCER OF THE STOMACH

**Definition.**—A malignant epithelial neoplasm of the stomach.

**Incidence.**—About one-half of all cancers arise in the stomach, and statistics of hospital *admissions* show 0.47 per cent. of gastric cancers. *Autopsy* statistics show 4 per cent.; Reiche's Hamburg statistics (1872 to 1895) show that 50.2 per cent. of all cancers are gastric, and that cancer of the intestinal tract, as a whole, forms 75 to 85 per cent. of all cancers.

**Regional.**—Deaths per 1000 population from cancer in general vary within rather wide limits: Amsterdam, 12; Berlin, 22.4; Geneva, 53; St. Petersburg, 15; New York, 19.3; and London, 28.7. Climatic conditions seem to have but little influence except that in tropical countries gastric cancer is more uncommon, *e. g.*, in Egypt (Griesinger). Regional differences where they exist are probably associated more with the manner of living and the diet than with the climate.

**Etiology.—Race.**—Gastric cancer is much less common in negroes. In 1880 the death rate in the United States from all cancers was: white, 25.9; negroes, 12.6.

**Age.**—The following results appear from 7000 cases gathered from combined statistics.

Ages.	Per cent.
10 to 20 years . . . . .	0.08
20 to 30 years . . . . .	1.5
30 to 40 years . . . . .	8.4
40 to 50 years . . . . .	18.0
50 to 60 years . . . . .	28.0
60 to 70 years . . . . .	28.0
70 to 80 years . . . . .	14.0
Over 80 years . . . . .	2.0

Congenital cases have been described (Williamson and Widerhofer), and Cullingworth performed an autopsy on a child, aged five weeks, in which gastric cancer was found. Osler and McCrae found 10 cases in the literature under ten years of age, and 13 cases between ten and twenty years. Probably more than 2 per cent. of all gastric cancers occur under thirty years of age; 80 per cent. or more between the ages of forty and seventy. With better methods of examination more and more cases are found among youths, which alters the ratio somewhat and brings the average down to earlier years.

**Sex.**—Of 20,000 cases collected from my combined statistics, 58 per cent. were in men. Welch gives the relation as five males to four females.

**Heredity.**—Opinions vary widely and statistics are very incomplete. In 1075 cases Snow found heredity in 167, *i. e.*, 15.5 per cent.; Schule gives 6.5 per cent. as hereditary; Lebert 7 per cent., and Roth 50 per cent. Of 2700 cases of gastric cancers, 12 per cent. showed an hereditary history. In the Royal Victoria Hospital, 24 per cent. gave a probable hereditary history, which was undoubted in 18 per cent. Cancer as a family affection perhaps occurs in 10 per cent. in all cases. At the same time, gastric cancer being in any case a frequent disease, there can be little that is reliable in such findings. Just how frequently the offspring of cancerous patients have subsequently developed the disease we do not know, and histories refer to relationships which are often too remote and indefinite to permit of accurate conclusions. Warthin has recently drawn attention to the marked incidence of cancer in certain families.

**Previous Gastric Disease.**—Long-continued irritation as a cause of cancer of the stomach is extremely dubious, and “badly used” stomachs seem to suffer no more than do those well treated. On the contrary, the development of cancer is often almost sudden when the digestion had previously been unimpaired.

**Chronic Ulcer and Cancer.**—Wide variations in the statistics are noted, because of many views and imperfect observations as to the diagnosis of ulcer. Cruveilhier discussed the relation of cancer and ulcer in 1839, and Rokitsansky soon after recognized its possible implantation in ulcer. Dittrich, in 1848, recorded 160 cases of cancer, of which 6 were of this etiology. Fütterer concluded that cancer frequently formed at the



edge of ulcers, especially where the part was most exposed to irritation, and in the pyloric region this development occurs in the lower margin. But if the position of the organ alters from dilatation or adhesions, other parts of the edges may be involved. Cancer develops in ulcer most frequently in the pylorus. (Fuller discussion of the subject will be found in the article on gastric ulcer.)

**Alcohol.**—Fifty-six per cent. of the Royal Victoria Hospital cases were habitués, and of these 20 per cent. were hard drinkers, and 30 per cent. drank moderately but constantly.

**Trauma.**—In 62 cases of cancer of the intestinal tract, Boas found 9 with a clear history of antecedent trauma, and *only 1 in gastric carcinoma*. According to some, and especially Fürbringer, trauma has a definite effect in aiding the development of latent cancers and increasing the rapidity of their progress. Kuttner and Lindner, after careful inquiry, found no history of injury in 66 consecutive cases.

**Auto-inoculation.**—Transplantation of cancer from a primary growth on the tongue into the stomach has been recorded by Klebs, Cornil, and others, but such instances must be very rare. The possibility of auto-inoculation from one cancerous tissue to another has been frequently noted, and surgeons have found it in the line of incision or of puncture in abdominal cancers infected from the original neoplasm.

**Pathology.**—Cancer of the stomach is a malignant epithelial overgrowth extending from the secreting cells of the mucosa to the other coats of the organ, and thence usually to the neighboring tissues, glands, and organs, or to distant parts by continuity, contiguity, and metastases through lymphatic and blood channels. It is nearly always primary in this organ.

**Secondary cancer** of the stomach is rare. Statistics show the proportion to be about 1.1 per cent. (*i. e.*, 5 cases out of 440), up to as high as 6 to 7 per cent. (Hale White). It arises either from contiguity or by metastases from distant viscera. Involvement by contiguity from the pancreas, liver, œsophagus, etc., is, of course, common and even transplantation from the tongue has been recorded, with the development of a secondary epithelioma of the stomach as a direct result of swallowing detached particles of the tumor.

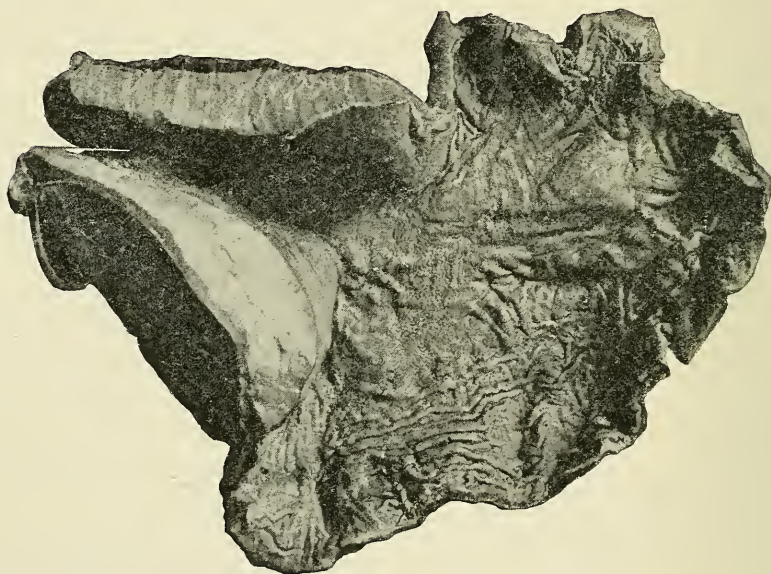
**Site of Growth.**—The pylorus (27.2 per cent.) and the lesser curvature (26 per cent.) are the most frequent sites. The frequency of the latter site accounts for the absence of obstructive signs in many cases of apparent pyloric cancer in which the *x*-rays show the patency of the pylorus. Mikulicz and Kausch, in 1900, mentioned the probability that 40 per cent. of cases of cancer of the stomach began in the lesser curvature, their observations depending on laparotomies and thus representing earlier types than are seen by the pathologist. As regards other sites of origin, two series may be quoted:

	Pylorus and lesser curvature. Per cent.	Cardia. Per cent.	Diffuse. Per cent.	Anterior or posterior wall. Per cent.	Greater curvature. Per cent.
Lebert and Hahn.	51	29	15		
Orth . . . . .	80	10	10	0.08	0.04

**Multiple Cancers.**—Occasionally several tumors are found in the same stomach, *e. g.*, Maurizio saw one case with cancer at both the pylorus and at the cardiac end, and Gierke reported a case with four cancers in one stomach.

**Relation of Cancer to the Changes in the Mucosa.**—The general mucosa elsewhere suffers coincidently with the progress of the cancer. Usually the superficial cells are fairly preserved or more goblet cells appear. The peptic glands become mucous glands, the border cells disappear more than the chief ones, and all are more or less surrounded by new small round cells. The mucous membranes may be completely absent in some places, due to the development of a general atrophic gastritis with small-celled infiltration, cysts, etc. The observation of Fenwick is noteworthy, *viz.*, that with cancers of organs other than the stomach there may be absence of normal acid gastric juice. Friedenwald and Rosenthal found a similar result in 9 out of 29 patients.

FIG. 5



Scirrhus carcinoma of pyloric end of stomach.

The cancer may be circumscribed or diffuse, *i. e.*, a fungating mass with a villous surface, or one that is more smooth and flat, and showing central dimples or areas of degeneration and ulceration, or else diffuse, extending mainly in the submucosa, which thus becomes thickened, giving to the whole wall a greater rigidity and firmness. The mucous membrane itself is usually roughened and in parts degenerated, while the organ is either large and dilated (if pyloric stenosis has occurred), or shrunken and the cavity much smaller than normal. In some of these diffuse cancers it may be impossible to distinguish the condition from a mere cirrhosis (interstitial gastritis) even by microscopic examination.

Two main types occur: The *scirrhous* and the *medullary*, although transition forms and mixed types are usually present in nearly all gastric cancers. They are, as a rule, hard tumors, due to the preponderance of fibrous tissue (where epithelium and stroma preserve the alveolar arrangement the name *carcinoma simplex* is used). The wall is thickened, the extension is often diffuse rather than circumscribed, and there is a tendency to scar formation in some places, while in others superficial ulceration is seen. Scirrhous cancers are slow growing, spread gradually into the surrounding tissues, especially the muscle. It is in this form that differentiation is sometimes difficult between cancer and simple chronic indurated ulcer or cirrhosis ventriculi. Scirrhous neoplasms are commonest at the pylorus, so that stenosis occurs, owing to the increasing size of the tumor or to shrinkage and rigidity at the orifice.

The *medullary form* is soft, very cellular, and thus on section shows more "juice." The progress is more rapid, degeneration and hemorrhage more common, and metastases are more readily formed. The glands especially are subject to invasion.

Papillary outgrowths of a special *adeno-carcinomatous* form are not uncommon. They form soft, fungating excrescences, oftenest at the pylorus, where they are sharply delimited at the duodenal end. Ulceration, necrosis, hemorrhage, and even perforation are apt to occur with this special variety.

The *colloid changes* may supervene in any form of gastric cancer. Diffuse thickening occurs from the presence of yellowish-brown, jelly-like, translucent fluid, which is seen occupying large or small spaces in the neoplasm. It is essentially a degenerative process of the cells and tends to invade the omentum, but not, as a rule, the intestines.

Myxomatous degeneration may occur in the fibrous stroma of any cancerous tumor.

*Squamous-celled cancer* commonly occurs about the cardia as the result of an epithelioma commencing in the œsophagus. It is rarely elsewhere in the stomach, except when secondary nodules form there either by transplantation from squamous-celled tissues (tongue, œsophagus), or by metastases from the œsophagus.

**Extension and Dissemination.**—The disease may be confined to the stomach, and may induce ulceration, degenerative changes, hemorrhages, etc. Extension within the stomach occurs chiefly by the lymphatics which run in the fibrous intersections between the muscle bundles. Here the course is vertical toward the serosa, which may also be involved. Cuneo has shown that the gastric lymphatics run toward the glands along the lesser and greater curvatures, more especially toward the pyloric end and in the adjoining portions of the great omentum, and thence through the cœliac glands on their way to the thoracic duct, thence to the supraclavicular region, as well as to the subclavian vein and the general circulation. In pyloric cancer the lesser curvature is rapidly invaded, and the lymphatics and glands become involved as far as the point where the coronary artery joins the stomach; here the lymphatics pass *from* the lesser curvature. The lymph nodes of the



greater curvature do not usually go farther to the left than a point near the median line. The fundus is almost devoid of lymphatics.

The disease commonly spreads in the subserosa and if degeneration occurs here, ulceration, and even *perforation* may follow with a consecutive peritonitis, general or local with adhesions, and perigastritis. Perforation is, however, an uncommon event (4.46 per cent.). In this way abnormal communications may form between the stomach and other viscera and tissues, *e. g.*, large intestine (gastrocolic fistula), small intestines, the anterior wall, pleura, pericardium, with admission of air and infected material into these cavities, the lungs and bronchi, with formation of abscesses, gangrene, etc.

Sometimes there is *partial healing*; scars form, although the process does not cease, and in other parts the neoplasm shows progressive degeneration. *Ulceration* occurs in a very large number of cases, probably in more than 80 per cent., and hemorrhages are common, the amount depending on the size of the eroded vessel or the degree of capillary oozing. Suppuration occurred in 4 of 40 cases observed by Boas.

Extension *outside* of the stomach occurs through continuity of structure, contiguity by means of adhesions, or by direct implanatation, chiefly, however, by the lymphatics and sometimes by the blood stream, especially the portal vein.

*Metastases* arise either from the blood stream or lymphatics. They may appear before any suspicion is aroused of the gastric origin of the neoplasm, as in Tilling's case in which a secondary node on the humerus was the first evidence of the gastric cancer. Often, too, the growths in the liver or peritoneum mask the original site. Metastases travelling by the *blood stream* most commonly enter the portal vein and liver. They also commonly extend to the peritoneum and omentum, the pancreas, spleen, kidneys, pelvis, bones, and lungs (especially the left). No organ is immune. The *lymphatics* bring metastases to the neighboring glands (85 per cent., according to Cuneo), chiefly those at the diaphragm, the perigastric and retroperitoneal glands, the extension occurring in the glands of the thorax and *supraclavicular* region as well as in the thoracic duct. Out of 556 cases the cervical glands were involved in only 21 (4 per cent.). Statistics show that in 2156 cases, metastases formed according to the following proportions in various parts of the body: glands, 44.1 per cent.; liver, 33.2 per cent.; peritoneum and intestine, 27.6 per cent.; pleura and lung, 7.3 per cent.; and pancreas, 7.6 per cent. In the Tübingen statistics (1891 to 1905) the distant glands were involved only in 7 out of 91 cases; in only 3 were the supraclavicular glands involved, and in the others the bronchial and mediastinal glands. Cancer of the cardia often extends to the œsophagus; that of the pylorus, on the other hand, rarely involves the duodenum.

The abdominal wall is at times invaded, chiefly through lymphatics of the obliterated umbilical cord, and great diagnostic importance attaches to the discovery of small secondary nodules in the subcutaneous abdominal tissue, especially about the umbilicus. Peritoneal cancer is common, and there may be ascites from various causes. The ascitic fluid may be serous, hemorrhagic, or chylous.

Secondary gastric cancer sometimes results from a primary growth in the stomach, *e. g.*, a cancer of the cardia may follow upon a pyloric growth, or, again, a pyloric stenosis may occur from compression by periportal cancerous glands, which become involved from a primary cancer of the cardiac orifice.

The general morbid anatomy reveals, as in any other cancer, marasmus, with brown atrophy of the heart and fatty degeneration of its muscle, brown atrophy of the liver, fatty kidneys, and not uncommonly degenerations in the spinal cord and peripheral nerves. Multiple thrombi associated with the marasmus, or arising directly from the neoplasm are sometimes found in the bloodvessels. General anasarca, anemia, and cachexia are added.

**Symptoms.**—These vary according to the stage of the disease, the situation, the extent and pathological character of the growth, and upon its direction of progression.

**Latency.**—The onset may be quite unnoticed either by patient or physician and the disease may be an accidental discovery at autopsy. Patients with gastric cancer may enjoy apparent health for months, with undisturbed appetite and digestion, and with maintenance of strength and nutrition even when extensive metastases are present, as described by Cheney and others. Cases occurring elsewhere than at the orifices are especially apt to be latent, although in cancers of the cardia when no obstruction has yet occurred, and no tumor can be felt, the course may be unobserved. Sometimes these cases simulate pernicious anemia. The examination for occult blood in the stools has aided in the diagnosis of cancers of the digestive tract.

**Onset.**—Symptoms usually begin with inexplicable “dyspepsia,” which does not respond to treatment. Following upon this are pain, loss of weight, and weakness, later vomiting, perhaps of blood, and the cachexia progresses to a fatal issue. The onset and persistence of dyspepsia in a man over forty years of age, who has previously enjoyed good health, is a suspicious circumstance. Sometimes the onset is apparently sudden, in the midst of health, or after some acute illness, or perhaps after a trauma. In one class of cases the onset is often characteristic, *viz.*, where *cancer follows ulcer* or is engrafted upon it. In many of these the diagnosis is obscure through the presence of hyperacidity, especially as the HCl may be in excess to the end, and with it hypersecretion and early motor insufficiency; perhaps all the more so because spasm develops at the pylorus with the hyperchlorhydria. The deficiency of HCl in these cases appears late, and lactic acid is correspondingly small in amount and only found late. Pain and hemorrhages are early signs in these cases and usually marked features.

**Early Digestive Symptoms.**—*Flatulence* is frequent, at first odorless. Later on with degeneration or ulceration of the neoplasm, the expelled gas has a fetid or foul odor from gangrene, suppuration, or the presence of organic acids. A *sensation of fulness* occurs even after very little food. *Anorexia* is common and early, and is apt to be progressive, although in many cases unimpaired until late in the disease. The appetite often shows caprice and an especial dislike for meat may develop.

The taste is altered and often perverted. Smokers commonly lose all desire for tobacco. Bulimia and dysphagia are rare. *Thirst* is definitely related to the degree of stenosis and to the motor insufficiency. The *tongue* is usually thickly coated, although at times clean for months; much depends on the condition of the teeth, gums and pharynx.

**Vomiting.**—This is very frequent, and occurs in 80 to 90 per cent. of all cases. It usually takes place late in the course of the malady, and is especially common in pyloric cancer, owing, of course, to the stagnation and dilatation. In Warren Lyman's statistics from the Royal Victoria Hospital, it was noted in 68.2 per cent. Sometimes it is early (in 7 out of 83 of our patients it was the first symptom, and in 34 it was very early). Acute fatal cases with rapid emaciation and repeated uncontrollable vomiting have been described. As dilatation becomes more pronounced the vomiting may be at longer intervals and then more copious, the vomitus being largely unaltered and mixed with mucus, blood pigment, detritus, etc., and having a foul or fetid odor from organic acids. Often three layers form in the vomitus when retention of food has existed, the uppermost frothy, the middle layer consisting of turbid fluid and partly digested foodstuff, while at the bottom there is a granular material with food in various stages of digestion and other matter foreign to normal digestion. When an ulcerating obstructive growth at the pylorus breaks down to create a new passage, the vomiting may cease for weeks and the motor insufficiency be temporarily relieved. Vomiting is much less frequent when the fundus or anterior wall is the original seat of the cancer. In 26 of our 83 cases, vomiting was either absent until death or until discharge from the hospital. When the cardia is affected alone, vomiting will be more of the nature of a regurgitation and with much mucus. It is, as a rule, preceded by nausea, salivation and digestive discomfort. As a rule, vomiting causes some relief to the general discomfort, but not much to the pain.

**Hematemesis.**—This is a common symptom, but occurs as an obvious sign in less than half of all gastric cancers. Chemical tests for occult blood, however, show hemorrhage to be much more frequent. It is important to distinguish between true coffee-ground vomiting and altered foodstuffs which have a similar appearance. This can be determined often only by chemical tests, by the microscope or the spectroscope.

The bleeding may occur from erosion of a large vessel, and be copious and even fatal, although this is rare (1 per cent., Welch); death may occur from hemorrhage without emesis. More usually there are small repeated hemorrhages, either from the degenerated tumor, or from superficial erosion of the mucosa. The blood oozes slowly, remains a long time in the stomach, and for this reason it is altered to hematin, giving to the contents the coffee-ground appearance. Tiny specks of very dark clotted blood, which frequently appear in the vomitus with cancer of the lesser curvature, are of diagnostic importance, coming from folds of the mucous membrane or in depressions of the neoplasm. This is often a very early sign of cancer, especially if associated with the Oppler-Boas bacillus. The blood, though sometimes pure, is usually



mixed with food. *Occult bleedings* are a very important finding, and form one of the most constant signs in the disease.

*Pus* is less commonly vomited, and if copious may be seen by the naked eye, or detected by its fetid odor. If in small amount, it may only be revealed by the microscope. It arises through degeneration and ulceration of the neoplasm, and its presence is important for diagnosis.

**Pain.**—This is usually preceded for a time by a mere sense of pressure and discomfort, especially after meals. It was the first symptom in 25 out of 83 cases in the Royal Victoria Hospital (31 per cent.), and was present in the gastric region in 75 per cent. In from 75 to 90 per cent. it occurs at some time during the progress of the disease. In Osler and McCrae's series 13 per cent. ran a painless course. In the Royal Victoria Hospital, 22 per cent. had no gastric pain (Lyman). The time of its appearance varies, sometimes only every few days or weeks, sometimes only at night, etc., while at other times it is constant. The degree of *intensity*, as a rule, is not excessive. There is painful distress or a dull ache, usually fairly well localized to the gastric area. Sometimes it radiates to the back and to the sacrum. If the cancer be at the cardiac end, the pain may be at the lower end of the sternum. In pyloric stenosis peristaltic, cramp-like pains occur, and there is a sense of unrest.

A relation between the presence of a tumor and the site of the pain does not necessarily exist. In some of our cases with diffuse infiltration of the stomach no pain existed, and pain was absent in at least one of each typical variety of regional disease. Cardiac cancer was especially free from pain. A relation to food may or may not exist.

**The Bowels.**—These are rarely regular and are usually constipated at first. F. Müller says that diarrhoea occurs in 35 per cent. of all gastric cancers and at times the two conditions alternate. Occult blood is present in the stools in probably over 90 per cent. of cases.

**The Urine.**—The quantity is usually diminished and the urine is concentrated according to the degree of gastrectasis and pyloric stenosis. The *chlorides* vary within wide limits, and *phosphates* are increased. *Nitrogen* is increased because of the great albumin destruction that occurs in gastric cancer (*vide* Salomon's test.) *Albumin* is frequently present although usually in small amount. *Albumoses* (peptonuria) have been found from time to time in gastric carcinoma. A certain diagnostic significance attaches to their presence. Aldor examined 56 unselected cases, and found albuminuria in every patient with fever and in 5 others in whom cancer of the stomach was present, and in one with cancer of the omentum. *It is merely a confirmative test.* *Indican and ethereal sulphates* are sometimes in excess and *acetone and diacetic acid* are sometimes present, and of no diagnostic import. *Volatile fatty acids* are in excess sometimes when cancer occurs with stasis and diminished HCl, but Sigel doubts the diagnostic value of this finding. The variations of these acids is too great to be relied upon (Rosenfeld). The presence of *sugar* in the urine implies the probable involvement of the pancreas or brain and perhaps of the liver.

**Nutrition.**—Emaciation is the rule; it is usually progressive, and is often the first symptom to arouse suspicion. The skin becomes lax,

dry, and wrinkled, the color earthy, sallow, and sometimes jaundiced. Cachexia supervenes, especially with motor insufficiency. There is nothing pathognomonic about the cachexia, and it has no diagnostic value in itself. Two exceptions are worthy of mention: (1) Sometimes patients run an advanced course with well-maintained nutrition. (2) Remissions occur, patients regaining some or much of their lost weight for a time, especially under careful lavage and diet, with encouragement. In cancer of the lesser curvature there is usually but little emaciation early in the disease. *Loss of strength* usually accompanies emaciation.

**Anemia.**—This is due to the toxemia, hemorrhage, and malnutrition, but the blood examination is of little value in the diagnosis. Usually there is moderate leukocytosis. The red cells are normal or much diminished, sometimes there is marked poikilocytosis, and the picture may resemble that of pernicious anemia. The hemaglobin is diminished. The average red count is usually about 2,000,000 per cmm.; the average hemoglobin is about 50 per cent. The absence of digestive leukocytosis has no practical diagnostic value.

**Fever.**—This occurs in about one-half or three-quarters of all cases, and at varying and irregular intervals. Sometimes there is an initial fever or irregular temperature during the course, and not uncommonly sudden elevations to 105° or 106° with rigors and as sudden a termination. At other times the type resembles that seen in malaria with chills and sweats. These irregularities in temperature are probably toxic, arising from absorption, if not due to complications, *e. g.*, peritonitis, pleurisy, etc., which should be looked for. Terminal pneumonia or pulmonary metastases often cause fever during the latter days of the disease.

**Adenitis.**—The neck may show enlarged *supraclavicular* lymph glands, especially on the left side. They become swollen, palpable, perhaps visible above the clavicle. The diagnostic value of this is doubtful and it may occur in any visceral cancer. Again, it is usually a late sign, not an early one. Sometimes, however, it is early enough to be of use, and therefore should be looked for.

**The Abdominal Examination.—Inspection.**—This is of great importance. Osler has drawn special attention to examination of the abdomen for unevenness of the furrows below the ribs, for fulness in the epigastrium, nodules in the skin and about the navel, peristalsis and anti-peristalsis, and, lastly, for a wide area of aortic pulsation. It is well to inspect the recumbent patient from behind the head of the bed. The tumor is often easily seen as it descends with deep respiration, and ascends with expiration, especially when the stomach is empty. With a full stomach a tumor may be pushed upward beneath the ribs or liver and be invisible. *Respiration* often has a marked effect on the position of the tumor, especially if it be localized to the pylorus, circumscribed and solid, and with adhesions to the liver. It may be accepted as a general rule that absence of respiratory mobility implies non-adherence to the liver. Cancers of the curvatures move readily, and may show fixation on expiration. This aids in the differentiation both of cancer of the stomach from that of other organs, and of cancer of the pylorus from that of the lesser curvature. Often tumors which descend with

inspiration may be held in that position during expiration. The changes of position depend on the size, the state, and the extent of the tumor. A large, wide tumor, adherent to the liver and yet extending below it, may be partly fixed even when the liver returns with expiration.

*Insufflation and inflation* have some influence on the situation of a neoplasm in the stomach. Inflation should be carried out with care. The writer saw a severe laceration of the mucosa under such conditions in a European clinic, where the autopsy revealed four or five linear tears from end to end of the organ. Pyloric tumors descend to the right, and those of the lesser curvature move backward and disappear because the larger curvature turns forward. By inflation, too, the position and size of the stomach are easily detected, and ptosis becomes more obvious, especially in cancer of the lesser curvature.

**Palpation.**—The examination should be made in various positions, and, if necessary in a hot bath, or under ether, in order to determine the size, shape, and situation, mobility, character, etc., of the growth. In the absence of a palpable tumor, the diagnosis often remains dubious. Sometimes a tumor is not accessible to palpation even when large, especially if (1) it is high up in the cardia, (2) if it is in the lesser curvature and fixed to that vicinity, or under the left lobe of the liver, or (3) if it is in the posterior wall of the stomach. Tenderness is common, in variable sites, and there are often tender points behind near the vertebræ. It is often possible to feel a hardness and the nodular character of a neoplasm and the knobs of cancerous masses with central depressions of degeneration (Farre's tubercles).

*Pyloric tumors* are the easiest of all to palpate, especially in women with lax abdomens and descended stomachs. Not infrequently one may feel the gurgling of gas through the pylorus. These tumors are sometimes quite movable, especially if non-adherent elsewhere and if confined to the pylorus. Sometimes they may be moved to almost any position in the abdomen, as in one instance in which the tumor could at will be pushed beneath the right costal margin, to the right iliac region, or across the epigastrium to the left of the median line, and even below the umbilicus.

**Gastric Rigidity.**—Boas has drawn attention to this symptom, although Creveilhier noted it more than half a century ago. The rigidity may exist merely as slight contractions of short duration confined more or less to the fundus, or as more marked tonic spasms of the muscle over a larger area, causing prominences of the fundus, and creating a sensation of pain to the patient, or, again, there may be still more decided contractions, which are both visible and palpable and are of longer duration. Gastric rigidity implies pyloric obstruction, and it is best observed with a full stomach.

**Percussion.**—Dulness or dull tympany may exist over a large tumor. There is increased tympany with gastrectasis. Inflation aids mensuration.

**Auscultation.**—Auscultation and auscultatory percussion are of doubtful value, although perhaps future developments may demonstrate their usefulness. The sign of the deglutition sounds, viz., delay in their occurrence and transmission to the ear, is of doubtful value, and certainly not pathognomonic. It is possible to hear, too, the gurgling of



gas through the pylorus. Friction from a localized peritonitis is sometimes audible.

**The Functional Signs and Analysis of the Stomach Contents.**—There is no one pathognomonic sign of cancer. The diagnosis is made from the symptom and sign complex. The signs vary greatly according to the site, size, and extent, shape, character, etc., of the neoplasm. Macroscopically the stomach contents show stagnation, fermentation, and poor protein digestion. Tumor fragments are rarely seen. Blood is common and sometimes there is pus. In typical cases three changes occur: (1) Motor power is impaired, (2) HCl is diminished or absent, (3) lactic acid is present.

The *motor power* is nearly always diminished early in all forms of gastric cancer and is a most important element in the diagnosis. It is not necessarily associated with dilatation, for a small rigid, cancerous stomach may equally well show motor insufficiency. It rapidly becomes more severe, especially with marked stenosis and insufficient hypertrophy of the muscularis. In cancer of the cardia it is less frequent than in cancer elsewhere. In cancer of the lesser curvature, motor insufficiency is slight at first until extension and infiltration have occurred, involving the pylorus, but not necessarily causing stenosis so much as preventing peristalsis and inducing a rigidity of the wall with insufficient pylorus. In cancer of the body of the stomach, more than 50 per cent. of cases show motor insufficiency because of the infiltration of the walls and their weakness through toxemia and cachexia. Where the wall is much infiltrated or where pyloric stenosis is marked, food may be retained for days or even weeks and the increase is usually progressive.

**Secretory Power.**—There is usually a gradual and progressive diminution of the free HCl until it is absent, and the ferments also disappear in part or entirely. This occurs in perhaps 80 to 90 per cent. of cases. One examination of the contents is never enough to form conclusions; it is the persistent diminution or absence of HCl which is significant. Variability in the amount of HCl secreted in gastric carcinoma is probably much greater than is commonly recognized, and the total acidity varies within still wider limits. Combined HCl is often absent. It is possible that much HCl is secreted but is quickly taken up by products resulting from the cancer. Emerson found that in ulcerating cancers certain basic substances were produced by autolytic processes, which combined with HCl. He believes these to be "hexone bases, the result of the digestion of the protein by a ferment furnished by the tumor itself." With cancerous dilatation we may get free HCl in an empty stomach, but not after meals. The important feature is the early disappearance of HCl with normal total acidity; later in the disease the total amount also falls off.

Ziegler, Sailer, and others have reported cases of hyperacidity with cancer of the stomach occurring early in the disease. The writer has observed repeatedly such cases in which the early hyperacidity lasted for more than a year before cancer was at all evident. In one of these cases the autopsy showed no sign of previous ulcer, but a carcinoma *en plaque*. In cancer of the fundus we get absence of HCl much earlier,

because the process is more diffuse, and therefore it affects the secreting glands more. In all cases one must distinguish between hyperchlorhydria and mere hyperacidity which is often due to organic acids as well. Hydrochloric acid may be present throughout the whole course of the disease, especially with localized tumors or where ulcer previously existed.

Absence of HCl is but one sign, and is of partial importance only; for it occurs, too, in gastric neuroses, catarrh, atrophy, etc., and in fevers, constitutional disturbances, cardiac disease, etc.

**Organic Acids: Lactic, Butyric, Acetic.**—The presence of *lactic acid* depends mainly on diminished motor power and lessened HCl, and therefore lessened digestion of albuminous foods, *i. e.*, lessened ferment activity because of atrophy of the glands. It may be introduced preformed into the stomach by the food, *e. g.*, bread, milk, fish, meat, etc., and for this reason Boas recommends a test meal of oatmeal and water. He gives this meal after having previously washed out the stomach, and removes it in the usual time.

Lactic acid is formed in the stomach, however, only under abnormal conditions, and is the commonest organic acid found in cancer. Its origin may be from acid producing microorganisms, *e. g.*, the Boas-Oppler bacillus, or from some special ferment associated with the cancerous tumor. Lactic acid is not pathognomonic of cancer, and may be present in many other conditions, though rarely in so marked a quantity as in cancer. Its *early appearance* in cancer of the stomach, together with a *diminution of the total acidity*, even before any signs of stenosis, is very important. Its absence is no proof that cancer is not present. Usually it is not an early sign, because it depends in part on atrophy of the glands and motor insufficiency. Still, these do sometimes atrophy *early*, as Hammerschlag and others have shown. The mucous membrane is sometimes destroyed even when a tumor is quite localized, and, *vice versa*, with extensive cancerous disease the mucous membrane is sometimes preserved. Hence the variations in time of the appearance of the lactic acid. Its constancy is very suggestive, for the persistent presence of lactic acid is rare in gastric diseases other than cancer.

**Ferments.**—Hammerschlag, in 1884, examined 280 patients with gastric disease, and found the peptonizing power (according to his method) below 15 per cent. in only 32 cases, of which 26 were cancer. In these there was no albuminous digestion in 23, and in the other 3 it was below 15 per cent. Oppler found that HCl secretion and ferment activity ran parallel, indicating that diminution of the pepsin cannot be regarded as an early sign of cancer. It is, moreover, not always present in cancer, and, *vice versa*, is present sometimes in benign stenosis with gastrectasis and in neuroses. The presence or absence of secondary atrophy of the glands is alone the decisive feature in the production of ferments. Early diminution of ferment production, even when HCl secretion is preserved, has been repeatedly observed.

*Occult bleedings* from the stomach or bowel should be carefully looked for as being one of the early and most important signs of gastric cancer. The benzidin test should be used. The importance of this sign in the diagnosis depends, however, on their persistent presence and on their

association with gastric subacidity. If occult bleedings occur in the stools, when HCl is present in the gastric contents, the diagnostic value is less, as ulcer could also produce similar results. If occult blood is not found in the feces, and there is gastric subacidity and good motor power, it argues against the presence of cancer.

**Microscopic Examination of the Stomach Contents.**—This is more or less valuable according to the period of the disease. Blood cells and pigment are commonly found. Pus cells vary in amount, and at least a few leukocytes can almost always be seen. The presence of blood or pus, or both, in the early morning lavage is of great significance. Bits of mucous membrane and of cancer tissue are not commonly found. A few cases are recorded, but being a late sign, this has but little value. The lavage water frequently has little shreds of torn mucous membrane, because the mucous membrane in cancer is friable. Examination of these shows widening of the submucous tissue at expense of the true gland layer, *i. e.*, glandular atrophy. It is often hard to be sure of this, however, because it depends upon which part of the mucosa accidentally comes away in the washings. Often more catarrh is evident, and this is not specific for cancer. Sahli, however, laid great stress on this, believing that a thorough lavage at night, and again of the empty stomach in the morning, would reveal in the last washing torn portions of the tumor. A true piece of tumor is the only single pathogenomonic sign of cancer of the stomach. But this means ulceration, and therefore is a late stage. Lubarsch regards early diagnosis by this means as impossible. Malkow found bits of tumor in the feces.

**Boas-Oppler Bacilli.**—These have been frequently found in the stomach contents in gastric cancer. They have been cultivated by Schlesinger and Kaufmann in pure culture on sugar agar, on beef peptone agar with the addition of cancer juice, and on grape sugar agar, although best of all are media to which blood is added. Hence they are frequent in coffee-ground contents. The average length of the bacillus is 6 to 8 $\mu$ , although it varies between 3 and 10 $\mu$ ; sometimes it occurs in long spirals and continuous threads, 1 $\mu$  broad. It is non-motile, Gram positive, stains a deep blue-red color with aqueous methylene blue, is facultative aerobic, and has no spores. It coagulates milk.

Schlesinger and Kaufmann demonstrated the formation of lactic acid from various forms of sugars by these bacilli, therefore they may be regarded as *one* of the excitors of lactic acid formation in the stomach, but only one; there are others, and therefore they are not specific for lactic acid formation. They have been found in 22 out of 70 cases of gastric disease; of these 22, 19 were cancers and 3 presented other conditions. Their absence does not prove the non-existence of cancer. Heichelheim emphasizes the findings in gastric contents of clots of blood with these bacilli, in the absence of HCl, as almost pathognomonic of cancer.

Ziegler has recently called attention to the microscopic evidence of stasis as important in the early diagnosis of cancer, especially the finding of the Boas-Oppler bacilli amid mucus which may plug the introduced tube, also food remains and numerous leukocytes. These early signs he



attributes to cancerous invasion of the lesser curvature, hence the rigidity, the lessened peristalsis, and slight stasis.

*Sarcinæ* are uncommon unless free HCl is present; therefore, as a rule they are only present when the cancer has formed on an old ulcer. The presence of *sarcinæ* is no proof that cancer is not present, although if they are in abundance the diagnostic value is of some importance as suggesting a benign rather than a malignant condition.

A few years ago Cohnheim recorded six cases of cancer with *trichomonas* and *megastoma entericum*. He attaches diagnostic importance to their presence in early stages before the lactic acid forms. They cannot live where lactic acid exists, and are hence more likely to be found in cancer of the cardia and lesser curvature, for in these cases often the lactic acid develops late. Others partially confirm these findings.

*Amæbæ* and *flagellata* are found in cases of cancer of the stomach in which no stasis exists, but in which an alkaline reaction obtains on the gastric surface, *i. e.*, non-pyloric cases. Cohnheim thinks them an early sign, and that they are found before the ulcerating tumor has become gangrenous. Later they disappear.

*Yeast cells* sometimes occur. *Meat fibres* are found because of delayed and lessened protein digestion. *Starchy foods* may be abundant, but are found to be more digested than the meats. *Fats* are likewise present.

**Diagnosis.**—Inasmuch as extirpation at the commencement of the disease is essential to a cure, the earliest possible diagnosis is necessary for rational treatment, and one must endeavor to determine not only the location of the disease, but the extent of its development, the presence or absence of complications, and the possibilities of satisfactory treatment. When possible, a diagnosis should be established before a tumor is detected, although from recent surgical statistics even this is not essential for a radical cure. Many tumors, even though palpable, are sufficiently localized for removal, and even when fairly large, a successful resection of the stomach has been accomplished. Then, too, many tumors feel larger than they really are, and *vice versa*. As regards palpation, it does not follow that because a tumor is not yet palpable that the disease is in an early stage. Huge cancers with adhesions and metastases may have already formed and be entirely covered and inaccessible to palpation, and, *vice versa*, an advanced condition may remain localized for a long time and grow slowly long after the diagnosis is made.

The main evidence in the early cases lies in the findings of functional disorder. There is no single pathognomonic sign of cancer of the stomach, and one must consider the whole symptom-complex, using for his purposes not only the history, but a careful examination of the symptoms, signs, the physical examination, the chemical and microscopic examination of gastric contents and stools, and such investigations require often prolonged, patient, and thorough observations. In spite of all there are numerous cases in which it is quite impossible to make a diagnosis. One general rule holds in most cases, *viz.*, *the absence of all gastric symptoms and signs is important evidence against cancer*. Penzoldt has well said that in individuals over forty years of age with gastric trouble, one should not rest until one has satisfactorily decided for or against cancer.

Klemperer advocates as a therapeutic test that elderly patients in doubtful early states should be placed on a rest cure with a protective diet for several weeks. If with this method improvement does not supervene, cancer may be strongly suspected.

**General Signs.**—When no tumor is evident one must rely on the age, family, and personal history, the history of the illness, especially its onset in the midst of good health, the anorexia, especially for meats, the hematemesis, weakness and emaciation in spite of apparently sufficient food, the motor insufficiency, and the results of chemical analysis and other investigations of the vomitus and contents from test meals, and upon the presence of persistent occult blood in the feces. In the stomach contents the cardinal features are evidences of motor insufficiency, the persistent diminution of HCl, the presence of lactic acid and of blood.

**Tumor.**—The possibility of palpating a growth depends much on the topographical conditions of the stomach and of the tumor, *e. g.*, cancers with adhesions, with extension upward of the growth, etc., may not be accessible to palpation. Where tumor is evident, one is called upon to decide (1) whether or not it be gastric, and (2) if gastric, whether it be of a cancerous nature or otherwise.

Certain *general tests* have been recommended as aids in the early diagnosis of gastric cancer before a tumor is palpable, although none of these have justified the claims originally made for them. The tryptophan reaction is based on the effect of chlorine or bromine to produce a red-violet color on the proteinochrom which forms as a result of the great albumin destruction. The test is expensive, lengthy and not constant, having failed in 13 out of 15 cases (Sigel), and having been found positive in other conditions, *e. g.*, ulcer. Bassler's and Kuttner's opinion was similar to that of Sigel. Oppenheim's test with acetic acid is equally inconstant.

Salomon believed an earlier diagnosis possible by testing the lavage water for nitrogen and albumin, his test being based on the idea that in gastric cancer owing to the great destruction of tissue, an albuminous serum is poured into the stomach. The stomach is first carefully washed on the evening before testing, after a preliminary non-albuminous fluid diet for twenty-four hours. On the next morning the stomach is washed thoroughly with normal saline solution (400 cc.), the same fluid being repeatedly used and then tested by Esbach's and Kjeldahl's tests. More than 20 mg. of nitrogen to 100 cc. or 0.5 gm. albumin suggests the presence of cancer. In negative cases there should be little or no turbidity with Esbach's reagent, and the nitrogen by Kjeldahl's method is not greater than 15 mg. Minkowski is not in accord with these views. Gerster, however, regards this test as useful in cancer of the lesser curvature without stenosis, unless the cancer has formed on an old ulcer, in which case the little HCl present would digest the albumin present. Reicher, Siegel, Tabora, and Zirkelbach confirm the test as being at all events of some value, especially as indicating an ulceration of the gastro-intestinal tract, although not necessarily differentiating malignant from benign conditions. Furthermore, it may assist in diagnosing cancer from chronic gastritis unless the cancer be of an early

diffusely infiltrating character. E. H. Goodman concludes that the test is not pathognomonic. He has modified the method, estimating the phosphates in the washings instead of the N and albumin, thus simplifying the test. Normal individuals show less than 10 mg. per 100 cc. In cancer the percentage usually exceeds 10 mg.

Gluzinski's test for the relative diminution of HCl has been mentioned. O. Reissner's contention that the diagnosis of gastric cancer is aided by the determination of the chlorides in the stomach contents, is worthy of mention. In gastric carcinoma the chlorides are apparently much increased, despite the fact that HCl is itself deficient, the alkaline cancer juices evidently themselves containing the chloride excess. The method of Lutke-Martius is employed, and while in other gastric diseases 100 cc. of gastric contents have a corresponding chloride value of 24 to 40 cc. of  $\frac{n}{10}$  silver solution, in carcinoma 50 to 70 cc. of  $\frac{n}{10}$  silver solution are required.

**Serum Test.**—Abderhalden's early pregnancy test, as modified and carried out by Doctors Bruère and Hardisty at the Royal Victoria Hospital, may be considered useful for certain cases of carcinoma, where the physical signs reveal any evidence of the disease. The cancer must be of such a size as to have caused a generalized blood reaction, *i. e.*, with antibodies or ferments in the blood. Pregnancy should be excluded. About 15 cc. of the patient's blood is drawn while fasting. No syringe should be used, but the needle placed in the vein should permit of the blood flowing into a sterilized tube under careful aseptic precautions. The blood is placed in the thermostat for five or six hours until the serum is well separated and the hemoglobin is removed by careful centrifugalization. Three hydrometer tubes are taken and sterilized. Into one 20 cc. of chloroform water (1 to 200) is added. A suitable parchment thimble (4 dialyses) is inserted, so that its surface comes in contact with the fluid. Into this thimble is placed 1 gm. of antigen, and 2 cc. of serum. If cancer be present a decided reaction should occur at the end of twenty-four hours. The other two hydrometer tubes are used as controls, placing into one of them 2 cc. of saline, instead of serum, and into the other 2 cc. saline with 2 cc. of serum (*i. e.*, without the antigen). All three tubes are carefully plugged and placed in the thermostat for twenty-four hours. The diffusates are each tested with ninhydrin for protein bodies. A positive reaction is indicated by the presence of a violet-blue color, which must be very decisive in order to call the reaction positive.

**X-rays.**—The method adopted at the Royal Victoria Hospital (A. H. Pirie) is as follows: A barium sulphate meal is given on an empty stomach. A cup of tea or coffee may be taken at 7 A.M., and the examination should be made before any food is taken. The stomach should then be found to be empty. In severe pyloric stenosis the stomach may be found nearly full, and this can be recognized before giving the barium meal by the horizontal line of the fluid in the stomach with the air chamber above it. The barium meal consists of a pint of thick butter-milk, to which 2 to 6 ounces of pure barium sulphate have been added. One ounce per 50 pounds of body weight should be allowed. The chemical



taste and grit of the barium sulphate can be got rid of by repeatedly washing it with hot water, and allowing the mixture to settle, then pouring off the clear water. This should be done on three successive days. The upper layer of the sediment should then be used. A patient with cancer of the stomach will frequently refuse to drink even half a pint of fluid.

*Carcinoma at the cardiac end* is usually made evident by stenosis at the oesophageal opening, and delay is observed in the entry of the barium into the stomach. This is best observed by screen examination.

*In the lesser and greater curvatures* carcinoma is recognized by a filling defect, with complete want of peristalsis in the affected part. The filling defect has a ragged appearance with indentations resembling the imprints of a child's finger-tips pressed into a mass of clay.

*Cancer of the pylorus* may cause unusual patency of the pylorus, with rapid evacuation of the stomach contents, or delay due to stenosis. When stenosis is well marked there are extra waves of peristalsis followed by periods of rest, during which no peristalsis goes on. Reverse peristalsis may be seen in stenosis of the pylorus.

If food is present in the stomach and the barium meal is superadded the junction of the two meals gives the appearance of a filling defect. The presence of this filling defect should be confirmed by two plates made at an interval of half an hour, and in both plates the essentials of the defect should be the same. Fluoroscopy and röntgenography should both be used for the diagnosis. Stasis in the stomach is simulated when the patient takes a meal before the barium meal has left the stomach. Thus if a barium breakfast is taken at 9 A.M., and lunch at 12 A.M., the barium of the breakfast mixes with the lunch, and may not leave the stomach for another five hours, so that at 4 P.M. barium will be present in the stomach. To avoid this possible mistake no food should be given after the barium meal until the stomach is empty, or until the fact of stenosis has been established.

**Differential Diagnosis.**—Two main types of condition may be considered: (A) Gastric cancer without evidence of tumor. (B) Gastric cancer with tumor.

A. *Where no tumor can be detected*, two classes of cases exist: (1) Those with little or no motor insufficiency. (2) Those with definite gastrectasis. (Cancer at the cardiac orifice, which will be dealt with separately.)

1. Where no motor insufficiency exists, the cases are easier to diagnose if lactic acid is found, for it is rare in the other gastric diseases that have no atony. The main diseases in this group are:

(a) *Ulcer* without tumor or stenosis.

(b) *Neuroses*.

(c) *Chronic Gastritis*.—The history of a cause (alcohol), the gradual onset and slower progress, with remission and exacerbations, are important features. The secretions are disturbed later in the disease, and the features are more local than constitutional. Hydrochloric acid is less constantly absent and is often diminished. Motor insufficiency is later, progresses less rapidly, and there is less gastrectasis; there is also less stagnation and occult bleedings are less persistent, if at all present.

(d) *Atrophy of the mucous membrane* (including pernicious anemia, primary atrophy of the gastric follicles, terminal stage of advanced chronic gastritis, cancer of distant organs, Addison's disease, etc.).

2. *Cases with gastrectasis* are harder to differentiate, because the lactic acid is so often present in gastric diseases with atony (other than cancer), and therefore its presence has less significance.

The main diseases to be differentiated are: *Scarred ulcer of the pylorus without palpable tumor* (which may lie beneath the liver or be too small for palpation). The history of previous ulcer, the longer duration of the malady, the presence of HCl (perhaps even in excess), the absence of lactic acid, the eructations of gas containing  $H_2S$ , and the findings of sarcinae, all suggest the benign condition; and the absence of cachexia aids in excluding carcinoma. Hypertrophic stenosis of the pylorus (Boas' stenosing gastritis) if acquired, is usually due to ulcer and gives signs similar to the above. Sometimes a *carcinoma developing on an old ulcer* must be differentiated, and the diagnosis is not always easy; indeed, often it is quite impossible. As a rule, there is a history of old ulcer and the symptoms change in character, becoming more persistent and resistant to treatment. There is, however, greater wasting, anemia and pain. Bleeding and perforations are not uncommon. HCl is present, often in excess, and there may be hypersecretion (continuous or alimentary). Gluzinski's tests are perhaps useful in these cases; at all events, if positive, they indicate the presence of cancer, and if negative, they do not prove its absence. Cancer developing on an ulcer shows a tumor more easily because of the usual perigastritis and pyloric spasm.

*B. When Tumor Exists.*—Two questions arise: (1) Is the growth gastric or extragastric? (2) If gastric, is it benign or malignant? The x-rays usually afford a satisfactory answer to the first question. One must use careful palpation, if necessary with the patient in a warm bath or under ether, unless, indeed, an exploratory laparotomy be undertaken. Minkowski suggested *inflation* of the stomach, and at the same time distension of the colon with water for differential diagnosis of gastric and perigastric tumors, though since the introduction of skiagrams *this method occupies a subordinate place*. Inflation or distension of the colon with water would displace gastric tumors upward, as also those of the spleen. Tumors of the kidney disappear behind an inflated colon. Tumors of the liver would vary according to size and position, while those of the omentum would be displaced downward.

**Growths Located Outside the Stomach.**—The tumors simulating gastric growths, but existing in reality outside the stomach, are mainly:

1. *Perigastritis*, with an exudate and perhaps adhesions about the pylorus, or the lesser curvature, may induce chronic pain with dyspepsia and even dilatation, simulating cancer. The main features against cancer are the long duration without sufficient corresponding emaciation and cachexia, the different chemical signs on analysis and the skiagraphic differences. (See "Complications of Gastric Ulcer.")

2. *Cancer of the Duodenum.*—This condition is rather rare. Schlesinger found only 7 primary cases in 25,000 histories. Rolleston could collect only 41 cases in the literature; of these, 8 were in the first portion,

5 in the first and second parts, 24 in the second portion, and 4 in the third portion of the duodenum; 10 were in females and 31 in males. Here the difficulties are great indeed; it may be impossible to diagnose the true condition. One may have diminution or absence of HCl. Lactic acid, on the other hand, may be present, as, indeed, may most of the other signs of gastric cancer.

3. *Omental or general peritoneal tumors* often cause difficulty in the differential diagnosis, especially if accompanied by ascites. These neoplasms are less mobile with respiration, and chemical tests on gastric analysis usually give negative results. The rectum should always be examined in doubtful cases of the kind.

4. *Peritoneal tuberculosis* with ascites may simulate gastric cancer with secondary peritoneal involvement. However, it occurs usually in younger subjects, runs a more protracted course, with exacerbations and remissions, and is accompanied by more persistent irregular fever. No occult bleedings occur. Dock has drawn attention to the value of cytological diagnosis of the fluid with its characteristic cells, in which mitoses are very common.

5. *Tumors of the transverse colon* usually give evidence of some degree of intestinal obstruction; the stools may be bloody and examination of the stomach itself is negative.

6. *Tumors of the gall-bladder* are situated in their appropriate place, are somewhat movable, and may by pressure upon the surrounding ducts cause early jaundice. At times, however, the differential diagnosis is extremely difficult. Adhesions in the neighborhood may cause pyloric stenosis and certain signs of gastric cancer. The absence of respiratory mobility may suggest a gastric cancer rather than one of the gall-bladder; but a test meal again is negative.

7. *Cancer of the liver* is usually secondary, and the tumor is less easily fixed with expiration than are tumors of the stomach. A satisfactory means of differentiating is, where possible, to place the hand above the tumor. Then, if the liver can be felt still higher, the tumor is probably gastric; at all events, it is not hepatic. The same is true if, with inflation of the stomach, the tumor alters its position. When the cancer of the liver is primary, the liver becomes large rapidly; jaundice is early and pronounced. The gastric signs are slight or absent, and there is no hematemesis or gastrectasis. Moreover, the usual signs after a test meal are not found.

8. *The pancreas*, either normal or pathological. When normal, it is deeply situated in the median line, fixed and immovable with respiration, and disappearing upon inflation of the stomach. When it is diseased, and especially when it is the seat of a cancerous growth, one may find clayey, fatty stools, even without jaundice. Jaundice may, however, be present from pressure of the growth upon the common duct. The portal vein may be pressed upon, and the resulting obstruction may give rise to ascites. There may be glycosuria, and, as a rule, the course is a rapid one. Armstrong recently reported a case in which a large pancreatic cyst simulated cancer of the stomach, even to the analysis of the gastric contents. The stools, however, had not been observed.



9. Other conditions which may simulate a gastric tumor are gumma of the left lobe of the liver, aneurism of the abdominal aorta, swollen glands about this artery, a movable kidney, and enlarged spleen, the last simulating a cancer of the fundus.

**Tumors within the Stomach.**—*Gastric tumors* arise either from carcinoma or sarcoma, cicatrized ulcer of the stomach or duodenum, with or without a perigastritis, thickened or spastic pylorus, fibroma, lipoma, or foreign bodies (hair ball, etc.). The differential diagnosis depends upon the history, the symptom-complex, and the physical examination:

1. *In scarred pyloric ulcers*, stenosis and gastrectasis occur with the results common to all cases of pyloric obstruction, but the history of previous ulcer, the long duration, the presence of a smoother and more movable tumor, the character of the vomitus with proteins well digested, and chemical findings typical of benign stenosis, usually render the diagnosis clear. There are, moreover, no metastases.

2. *A hypertrophic stenosis of the pylorus* is usually acquired, but occurs, however, oftenest in early infancy. The cases late in life usually have diagnostic features common to scarred pyloric ulcers with obstruction, with which, too, they have usually a causal connection. Simple hypertrophy is undoubtedly rare. Sometimes it occurs with mere hypersecretion. One relies on the history and duration, the chemical analyses, and absence of general signs of cancer. Occasionally it may be impossible to differentiate the two conditions.

3. Spasm of the pylorus may possibly induce gastrectasis, and if so will manifest few if any of the signs of malignant disease. The condition will be of long duration, with exacerbations and remissions, and will present no chemical signs in the gastric contents of malignant disease nor occult bleedings in the stools.

4. *Fibromata and lipomata* can only be inferred and not definitely diagnosed in the present state of our knowledge.

**Regional Diagnosis of Tumors within the Stomach.**—Certain differential features are useful to determine *the exact site* of the neoplasm in the stomach.

*Cancer of the lesser curvature* usually presents achylia from the beginning. There is less motor insufficiency until cancerous infiltration occurs. Peristalsis is absent, but one may get tonic contraction of muscle (gastric rigidity). When the neoplasm extends to the pylorus, we get pyloric rigidity with insufficiency, *i. e.*, a paradoxical condition of motor insufficiency with pyloric insufficiency, which may be tested by inflation. It is usually a late sign. Cancer of the lesser curvature is palpable only if ptosis exists or if the tumor has attained a considerable size. The weight is often maintained for a long time, because there is less motor insufficiency. Salomon's test has special value in cancer of the lesser curvature without pyloric stenosis, although it is useless if the cancer has developed on an old ulcer, because small amounts of HCl will digest the albumin. Estimation of the ferments aids regional diagnosis sometimes. The fact that the fundus yields pepsin and rennin, while the pylorus gives merely pepsin, affords an opportunity by ferment estimates of locating the probable site. If rennin is preserved while

the pepsin is relatively diminished, it implies *involvement of the pylorus*, while if both are lessened it signifies a tumor of the *fundus*.

*Cancer of the Cardiac End.*—Statistics of the Middlesex Hospital (1854 to 1904) recorded 227 cases of cancer of the stomach, of which 19 had their origin at the cardia; 13 were in males and 6 in females. Certainly the condition is uncommon, and many cases supposedly originating in the cardia have probably commenced in the œsophagus. Fagge's views expressed in his reports from Guy's Hospital on the frequency of gastric cancer suggests that "almost all cases that have been set down as examples of cancer affecting the cardia have really been instances of cancer of the end of the œsophagus extending into the adjacent parts of the stomach . . . . Indeed, on *a priori* grounds we should expect that a part at which the digestive tube is opening out into a large cavity should have little or no tendency to be affected with the disease in comparison with the narrow passage above it." The type of cancer originating at the cardia is usually adenocarcinoma. Sometimes a cardiac cancer with stenosis is accompanied by separate cancer of the pylorus, and sometimes, too, cancer of the cardia is accompanied by a secondary stenosis of the pylorus from pressure of metastatic periportal glands.

*Symptoms of Cancer at the Cardia.*—Being usually inaccessible to palpation they remain latent for a long time. An interesting example under personal observation occurred in a man, aged forty-eight years, whose death occurred within four weeks of the onset of the symptoms. His earliest symptoms were those of abdominal distension, swelling of the left leg, and some weakness. Careful inquiry elicited the fact that while for three weeks he had felt general abdominal pain with some anorexia, there had been no other subjective evidence of gastric disease. At the end of three weeks there was enormous distension from ascites, and he died two days later, sudden abdominal pain appearing; the autopsy revealed a primary cancer of the cardia, with secondary involvement of the peritoneum.

Apart from the general signs of malignant disease, there is dysphagia and distress immediately after meals with regurgitation of food and mucus. Pain comes on at once after food, and is usually greater in this form than in cancer of the pylorus, and often there is tenderness on percussion or pressure over the xiphoid cartilage. As obstruction develops at the lower end of the œsophagus, there is at first some difficulty in the ingestion of solids, and their deglutition is assisted by liquids. Oppression and discomfort usually supervene. Later on, even soft foods are swallowed with difficulty, and finally only liquids can be taken into the stomach. When the obstruction is greatest, all food is ejected with retching. Vomiting is less frequent than mere regurgitation. The passage of a tube meets with an obstruction near the cardiac orifice. The withdrawal of blood on the end of the tube is of great diagnostic value. Motor insufficiency is usually slight and lactic acid fermentation need not exist. The delay of the deglutition sounds is not a reliable sign.

*Course and Duration.*—Dyspepsia, loss of flesh, pain, and vomiting, in the order mentioned, mark the progressive course of the malady. As a rule, the disease has few or no remissions, and the progress to a

fatal ending is uninterrupted. Sometimes temporary improvement, both subjective and objective, occurs with marked gain in weight, color, appetite, and even strength. These ephemeral remissions often render the differential diagnosis from chronic gastritis most difficult. Sometimes there is an acute rapid course with vomiting, and a fatal termination in a few weeks, with carcinosis. Schweppe, in 1890, collected 22 cases from the literature, and since then numerous others have been observed.

The *duration* varies according to the nature of the neoplasm, its site and extent. Non-obstructive scirrhus cancers are the slowest to develop, while medullary cancers and those causing stenosis of the orifices proceed more rapidly. Some authorities regard the cases which occur in youth as being especially rapid, but statistics do not all bear out this view. The average duration in cancer of the stomach is about one year, although some patients live longer than three or even five years. Death occurs either from marasmus, metastases, or complications (hemorrhage, perforation, peritonitis, sepsis, pneumonia, etc.).

**Prognosis.**—This is always extremely grave, and few cases are cured. The medical treatment is purely symptomatic, and permanent relief is only to be had from complete resection of the malignant tissue. This is unfortunately suitable in but a limited number, although with improved methods of early diagnosis and better surgical technique, the hope of cures shows a satisfactory advance in the last five years out of all proportion to the gains in all previous years.

**Treatment.—Medical.**—This varies chiefly according to the situation of the growth and the functional signs. While the radical treatment is essentially surgical, there is much to be said for the medical treatment, which may be of great benefit, even though it cannot in any sense cure the condition. It is especially called for in inoperable cases, or when for some reason operation is refused, and finally in those cases in which a palliative gastro-enterostomy has been performed and the physician is called to aid in alleviating the distressing symptoms which inevitably occur even under such conditions. The cases may be divided into (1) those with obstruction at the cardia, (2) those with pyloric stenosis, and (3) those in which no orifice is involved, but the body of the stomach is the main site of the neoplasm. The treatment is dietetic, mechanical, and medicinal.

In *cancer of the cardia*, especially with the development of obstruction, soft or liquid diet is essential, and solids should be avoided. Small amounts with frequent feedings are better than large meals, and will better prevent regurgitation, pain, and distension of the œsophagus. Mechanical treatment plays but little part, and the use of a sound for therapeutic purposes is of questionable value. There is great danger of increasing the distress by injuring the parts, although if a tube of proper size and consistence be carefully employed it sometimes gives freer passage to food for a time and relieves symptoms.

In *pyloric stenosis with gastrectasis* the diet should not be too restricted. As a rule, liquid foods which are easily assimilated are best borne. But one should be largely guided by general principles, consulting the preferences of the individual. The meals should be small, frequent, and



non-irritating. Hydrochloric acid being usually deficient, meats and albuminous foods should be restricted. When administered they should be finely divided, and free from cartilage and other ingredients difficult of digestion. White meats are preferable, chicken, game, and pigeon, also veal and beef in small amounts, and fish. It is well after the use of proteins to give small quantities of dilute HCl (unless HCl be present in the gastric secretion). Fleiner recommended the use of sauces containing HCl, *e. g.*, beef juice with warm water, to which ten drops of dilute HCl is added. This is theoretically of little value, as it cannot duly replace the deficiency, yet experience teaches that it often aids digestion. The same may be said of the use of pepsin and pancreatin, which, despite the observations of Chase and others, give a sense of comfort to the patient after the food has been taken. Instead of HCl, Eichorst uses phosphoric acid after meals, and if pain be present, he recommends the addition of small doses of codeine.

It is a delusion to believe that the liberal use of albuminous foods prevents decomposition of the albumin of the body. The more a cancerous patient gets, the more he destroys.

The finer vegetables, preferably mashed, may be used in relatively large amounts, avoiding those with shells, skins, fibres, etc., as also those which induce much fermentation. Stale bread may be allowed, as also gruels, vegetable soups, and thin, farinaceous preparations like rice, macaroni, barley, tapioca, sago, and oatmeal. Stewed fruits are also well taken. Milk with coffee, cocoa, cereals, etc., may be employed, as also buttermilk and koumyss. Infant foods are often taken with relish and should be tried. Butter is the best borne of all the fats.

As beverages any of the ordinary drinks may be given, but in limited amount because of the motor insufficiency, and also light wines, brandy, and whisky in small amounts and diluted. Thirst is often troublesome and if not relieved by the moderate use of fluids, saline enemata may be used, one-half to one pint being injected night and morning.

*The Mechanical Treatment.*—Lavage with plain water, as a rule, alleviates the distressing local symptoms, and may help to increase the appetite and stimulate the secretions. The washing should be thorough at each occasion and unless gastrectasis be extreme, one lavage daily will suffice, before the last small evening meal or in the early morning. Cohnheim introduces two or three ounces of warm oil through the tube after the completion of the lavage, thereby giving still greater relief to the local distress.

*In cancer of the body of the stomach*, where motor insufficiency is but little evident, the main treatment is dietetic, the food being administered as described in pyloric stenosis. In these cases mechanical treatment is less indicated.

*Medicinal Treatment.*—No medicine is of any great value. Orexin in doses of 5 grains (gm. 0.3) may help the appetite, as also may an infusion of condurango bark. Alkaline mineral waters before meals sometimes stimulate the secretions, while HCl after meals helps protein digestion. For the *vomiting*, especially of blood, rest to the stomach is essential. Nutrient enemata may be given, and then careful feeding

by mouth may be begun with small quantities of fluid. For the ordinary vomiting, lavage is the best form of treatment.

*Diarrhœa* should be treated by a proper diet when possible, and by the use of lavage to remove irritating substances, which are the probable cause of the condition. For the *constipation*, aloes, rhubarb, and cascara are the most effective remedies. Enemata should be given when the condition is aggravated, but these should not be continued for too long a time. Authorities differ as to the use of saline purgatives, and doubtless in individual cases their use will have different effects.

For the *pain* wet compresses upon the stomach, lavage, and the use of spirit of chloroform may be of value, and it is only in the extreme cases that morphine should be employed.

**X-rays.**—*X-rays* and *radium* have been used with varying success, but with no results sufficiently brilliant to warrant favorable statements. When, however, extirpation of a cancerous tumor has been attempted, the use of radium is undoubtedly of value in preventing the rapid recurrence of the neoplasm, if not in entirely healing the disease.

The use of *thymus extract* hypodermically has been suggested, based on the researches of Gwyer, Rohdenberg and others, and a certain measure of palliation has resulted. No records, however, have shown that a cure may be obtained by using any of the internal secretions.

**Surgical Treatment.**—Statistics of surgical treatment are still to be regarded with reserve. Alexis Thompson has emphasized the frequency of non-malignant fibromatosis simulating cancer, thus exposing many of the difficulties of diagnosis and inaccuracy of reports on surgical "cure" of cancer.

Two measures must be considered: 1. *Exploratory operation for diagnosis*, and not merely to confirm the diagnosis. When a tumor is present and the gastric analysis gives every indication of cancer, it is but idle curiosity to explore, unless it is known beforehand that some chance of giving relief exists. The object of exploration is to *make* the diagnosis when great suspicion and doubt exists as to the possibility of cancer. If in such cases a reasonable suspicion exists, the earlier discovery which an operation thus permits, gives to the patient the better chance of radical surgical cure, and as such, exploration is not only justifiable but advisable in the extreme. Delay under these conditions, to await further evidence, implies unnecessary waste of time. At other times it may seem uncertain (even when a tumor is palpable) whether extirpation is advisable and possible, and under these circumstances exploration is justifiable.

2. *Operation for treatment*, either curative or palliative. The cases which promise successful results are as follows: (1) Those in which the neoplasm is well localized and movable. One should be guided chiefly by the character and extent of adhesions, those which are not extensive and uninfiltrated being most satisfactory to deal with. Hence, Ewald's contention that one must explore before deciding on further operative interference. (2) In the stomach itself the course of the lymphatics has an important bearing on the prognosis and treatment. The studies of Cunea have shown that the lymphatics along the lesser curva-

ture run for the most part from the pylorus *toward* the cardia, while those along the greater curvature and fundus lead toward the pylorus. Thus in operations for gastric cancer, the extent of removal depends largely on the site of the growth. Pyloric cancers do not tend to spread to the fundus and greater curvature, and these parts, therefore, do not need to be included in the resection. On the other hand, the lesser curvature should be removed, at all events as far as the gastric artery (Mikulicz's point), and along the greater curvature as far as Hartmann's point, which delimits the lymphatic extension along that line (Hartmann-Mikulicz line of section). Toward the duodenal end, the resection should be made one inch clear of the pylorus, this being the extreme limit of secondary involvement in nearly all cases. Even in cancers of long duration the neighboring glands are sometimes left free.

*Special Considerations.*—*Infiltrating adhesions* are a contra-indication and a dangerous complication in operations. It has been estimated that 73 per cent. of such cases die, and the remaining 27 per cent. recover because the adhesions were slight, and probably non-infiltrating.

*The Size of the Tumor.*—The fact that a tumor is externally palpable is no longer regarded as a contra-indication to surgical treatment. In fact, the size of the tumor is less important than is the presence of adhesions. Many large tumors may be capable of successful removal because they are free from adhesions and metastases, while many primary tumors which have remained very small may have involved neighboring glands and organs. Metastases in the liver, for example, may be large and numerous even when the primary local gastric neoplasm is small, movable, and non-adherent.

*Complications* form another important contra-indication, *e. g.*, arteriosclerosis, fatty heart, and tuberculosis.

Statistics from the various surgical clinics are published from time to time, showing the average duration of life after operations of various kinds. These, of course, have no value as regards the selection of operation. To know, for example, that after a gastro-enterostomy, 33 per cent. died is of little value. Such an operation is merely palliative and the cancerous growth proceeds. Immediate results depend largely on the technique and the condition of the patient at the time of operation, both of which factors determine the success of operation and the ultimate duration of life. The only operations which are curative are those which remove the entire diseased parts.

*Methods.*—*Gastrectomy* was first successfully performed by Billroth in 1881, when a partial operation was done, while complete removal of the stomach was first attempted by Connor, of Cincinnati, in 1883, who, although unsuccessful, paved the way for the later good results of Schlatter, of Zurich, in 1897, who performed a complete gastrectomy with recovery. The œsophagus and jejunum were united and the duodenal opening closed. Since then gastric operations have become matters of everyday experience, and the European clinics especially give large series of cases with statistical results (Kroenlein, Mikulicz, Kocher, Czerny, Robson, and Moynihan).

Partial gastrectomies result in improved motor power; secretion is



not altered, as a rule, although sometimes HCl returns and lactic acid disappears when stagnation ceases. Modern surgery advocates partial gastrectomy as the best of all operations, as yielding less mortality, and because it results in better health, comfort, and appetite, and in general well-being, with the best chances of complete recovery. Mayo quoted MacDonald as having found 43 undoubted cures from operation. Kocher, in May, 1907, reported 95 cases, of which 13 were well, and 4 others, although cured of cancer, had died later on from other diseases, *i. e.*, a total of 17 (19.3 per cent.) cured. Le Riche has recently tabulated cases, of which 89 cancers with gastrectomies were cured for a period varying from five to sixteen years. Of these, 1 had survived sixteen years, 34 from five to ten years, and 5 at least ten years. These cases include all kinds of cancers anatomically, mostly from the pyloric region, but one had been at the cardia. In a total of 1366 collected gastrectomies for gastric cancer, the mortality was 25 per cent. Peterson and Colmers recorded 30 cases with 20 per cent. of cures (Lisbon Congress), adding that all these patients were then in good condition, performing ordinary daily work with no gastric complaints, with an easy digestion, and that even the distaste for fats and meats had disappeared. The secretions, however, were feeble. In all there was deficient HCl; some still have lactic acid, but the motor power was excellent. Undoubtedly, such statistics are more than favorable, and in view of general experience, extremely optimistic. Much probably depends on the virulence of the cancerous growth and the susceptibility of the individual.

*Remote Results.*—Evidently the mechanical, physiological, and chemical functions of the stomach can be taken up by the parts left behind. Sometimes the œsophagus or small bowel dilates to form a kind of reservoir. Digestion is carried on well by the intestinal juices and pancreatic and hepatic secretions, and absorption takes place in an apparently satisfactory manner, and thus perfect health is maintained. Hayem has observed “hypopepsia” after years in patients in whom cures have resulted following operations for gastric cancer.

*Palliative surgical treatment* is employed in some inoperable cases when the strength of the patients permits surgical interference if the indications therefore justify the undertaking. Cure is not aimed at, but merely a relief of certain symptoms and fulfilment of certain requirements for improvement of local and general conditions. The indications for gastro-enterostomy are, briefly, pyloric stenosis from a cancer which cannot be removed, either because of its extent or owing to the involvement of too many neighboring glands, hour-glass or other deformity involving stagnation of food and its complications, hemorrhage which is persistent, and uncontrollable vomiting, whether from retention or from general causes. It is further indicated in some cases as a temporary measure prior to the more serious operation of gastrectomy, when patients are too weak to undergo the latter operation immediately.

In any doubtful cases with adhesions to the neighboring organs or pressure of inflammatory tissues about the pylorus, a gastro-enterostomy may not only relieve, but cure. In a patient whose condition was recently reported by my colleague Garrow, a large indurated and

nodular mass was found at operation involving the pylorus. It had been tucked up underneath the liver, and thus was not palpable; a second mass extended along the lesser curvature, while the glands in the lesser omentum were enlarged, although not indurated, as was the mass in the pyloric region. The condition was regarded as undoubtedly of a cancerous nature, and a palliative gastro-enterostomy was performed. One year later the patient was seen again in excellent health, suggesting the probability of some lesion other than a malignant one. Operation should be delayed when there is little gastric disturbance and when there is great weakness. Cases with small stomachs and infiltrating cancers should be let alone.

The beneficial results of gastro-enterostomy are often marked. Patients may gain in weight, the appetite may increase, vomiting and pain diminish, and general improvement follow for some months. Comparative comfort may thus be attained. In other cases, however, results are discouraging and the patients decline rapidly; the rapidity of growth in the neoplasm is marked, even closing the artificial opening.

*Gastrostomy* is indicated where food cannot be properly taken into the stomach, either through cancer of the œsophagus or of the cardiac end of the stomach. The operation should be done early to obviate the great weakness resulting from defective nutrition, and thus the ordinary dangers from a comparatively simple operation may be avoided.

### ACUTE GASTRITIS

**Definition.**—An acute inflammation of the gastric mucosa with varying degrees of local and constitutional disturbance.

**Classification.**—Various types exist dependent upon the different etiological factors. Clinically there are three main types: (1) Acute simple gastritis (primary and secondary). (2) Phlegmonous gastritis. (3) Toxic gastritis (mild and severe). *Anatomically* one may add two other forms: (4) Mycotic gastritis. (5) Diphtheritic gastritis.

**Acute Simple Gastritis.**—**Definition.**—This is an acute catarrhal inflammation of the gastric mucosa, frequently accompanied by excessive secretion of mucus, desquamation of epithelium, and a resulting disturbance of digestion.

The condition is more often wrongly than correctly diagnosed, and in numerous instances a functional disturbance with slight temporary atony, or a neurosis, is misnamed gastritis. The term gastritis should be restricted to those patients in whom definite evidence of gastric inflammation exists, and should not be applied to temporary disturbance of function resulting from slight indiscretions in diet. Certainly one often cannot decide clinically whether or not a true inflammation exists, for there are very few pathognomonic symptoms and signs of a mild simple gastritis. The autopsy room reveals often enough an acute inflammation of the gastric mucosa without a previous history of gastric symptoms, and, *vice versa*, where much disturbance of digestion may have occurred and when even much mucus has been secreted, the inflammatory lesion may be very slight indeed.

**Etiology.**—The condition is either primary or secondary.

*Primary Acute Simple Gastritis.*—Predisposing and direct causes exist. The former are numerous: faulty hygiene, the hot summer season, malnutrition, anemia and other circulatory disorders, constitutional and metabolic disturbances, and infectious diseases. Previous chronic gastritis predisposes to acute attacks. Individual susceptibility is an important factor, and perhaps heredity plays a part. Age, too, has much to do with susceptibility, infants being peculiarly liable.

The direct causes are mechanical and dietetic, thermal, chemical (toxic), or parasitic (vegetable or animal).

1. *Mechanical causes* are mainly associated with errors in diet, *e. g.*, irritating food or drink, too bulky or coarse food, or excess after prolonged fasting. Food when taken in too large an amount may remain undigested, and induce fermentation or putrefaction, so, too, the shells of some vegetables, the stones and rinds of fruit, foreign bodies, hair, etc.

2. *Thermal Causes.*—Food and drink if at extremes of temperature may induce gastric catarrh, so also the external application of heat and cold; and extensive burns on the body. Whether or not “cold” is a cause in itself is doubtful.

3. *Chemical causes* are perhaps the most frequent. Alcohol is the commonest factor and leads to the disease in its most typical form. Those unaccustomed to alcohol are the most liable, and the inflammation arises either from irritation from the amount taken, or in the case of some wines because of the acid produced by acetic fermentation. In children unripe fruit is a common cause. Any chemically strange substance if toxic, in strong enough concentration and of sufficiently irritating character, will induce a gastritis, *e. g.*, alcohol, acids, alkalis, salts of the heavy metals, calcium chloride, and certain drugs, *e. g.*, salicylates, the bromides, iodides, arsenic, mercury, phosphorus, copaiba, etc.

Decomposed *pus*, as in gangrene of the lung when the irritating sputum is swallowed, and, indeed, any decomposed albumin may directly or indirectly induce the disease. *Foods* if tainted or decomposed (“crapulous gastritis”) bring about an inflammation directly through the action of fermentative or putrefactive agents; so also does stale beer. *Toxalbumins* form another group of agents. They are secreted in the stomach from a variety of sources, *e. g.*, in Asiatic cholera. Such agents may be denominated as autotoxic causes, and are present in numerous diseases, (uremia, diabetes, gout, cholemia, and also in burns).

4. *Parasitic Causes.*—*Vegetable Parasites (Bacteria).*—The invasion of bacteria is one of the most common causes of acute gastritis—hence its frequent presence in the various acute infections of all kinds. The colon bacillus is one of the most frequently found organisms, and in cases where it occurs in the course of acute infections is often regarded as the cause of the secondary gastritis. In all such instances the origin of the gastritis may be largely chemical, and due to the products of the bacteria. An epidemic form of gastritis has received attention from various writers who regard this ill-understood condition as originating in some form of microbic infection. This “gastritis infectiosa” is regarded by some as a special disease.



*Animal parasites* are commonly associated with a true gastritis, although it is by no means a necessary feature of parasitic invasion of the stomach. The ascarides, the tænia, and even the oxyurides may induce an accompanying simple catarrh of the gastric mucosa, as may also the diptera, flies, and larvæ of various kinds.

*Secondary acute gastritis* develops in the course of many infectious diseases, and may indeed be the main initial symptom to arouse suspicion of a grave infection. This is especially the case with children. In various pulmonary diseases when degenerated or decomposed tissues and exudates are introduced incidentally into the stomach an acute catarrh results. Ellis records a hemorrhagic gastritis due to a swallowed laryngeal pseudomembrane, which also obstructed the pylorus. As an accompaniment of various intestinal diseases, acute renal and cardiac disease, etc., acute gastritis is not uncommon.

**Pathology.**—The size and shape of the stomach are not usually altered. There is a more or less diffuse redness and swelling of the mucosa, with congestion or patchy hemorrhages and an excessive quantity of mucus. The pyloric region is most frequently involved.

Microscopically, muciparous, cylindrical epithelium covers the free surface of the mucous membrane as well as the relatively deep stomach cells. The glandular epithelium itself shows granular degeneration, with more or less fatty change and atrophy, and the lumen contains debris, for the cells themselves have desquamated. Hyperemia occurs either diffusely or in patches, and there are more or less minute hemorrhages. Leukocytes have escaped from the surrounding dilated capillaries, and a certain amount of small-celled infiltration is evident in the interstitial tissue. The solitary lymph follicles may be swollen, and sometimes burst on to the surface, leaving minute ulcers. The resulting changes affect the secretion of mucus and gastric juice, and alter the general functions. Hence disturbances of the sensory, secretory, absorptive, and motor gastric functions occur.

**Symptoms.**—These depend much upon the cause. Usually within a few hours, or at most a couple of days after action of the causative agent, there is gastric discomfort, fulness and sense of pressure or pain, with pyrosis, nausea, and vomiting. Often an initial rigor or chilliness ushers in the disease. The patient complains of a curious taste, sometimes bitter; there is also salivation. Thirst is a prominent feature. Nausea usually precedes the vomiting and occurs with food or at the mere thought of it; vomiting itself occurs early and gives relief. The vomitus contains undigested food, mucus, bile, and sometimes streaks of blood. It is bitter in taste, and, as a rule, of a foul odor. Cardialgia, pyrosis, and waterbrash add to the distress. The teeth are set on edge and the burning acid fluid irritates the pharynx and œsophagus. There is hiccough, and eructations of gas, either bitter or tasteless, are common. Pain is almost always present, slight or severe, and sudden or gradual and progressive. With all these subjective sensations are numerous nervous phenomena, headache, dizziness, and depression of spirits.

**Signs.**—The patient shows more or less prostration, and, if the condition be at all severe, the face is pale, the extremities are cold, and he breaks

out in a cold and clammy perspiration. The pulse is at first increased, later lessened in rapidity. Fever, if present, appears early, and is usually slight, although sometimes, when there is an initial chill, it may be high and accompanied by herpes; often, indeed, there is no fever throughout, but when, on the other hand, fever persists for days, one should examine carefully for some other factor to which gastritis may be merely secondary. In the so-called epidemic or infectious gastritis, the fever remains high for days, sometimes even for several weeks. The condition differs otherwise but little from ordinary simple gastritis, although an enteritis is a much more frequent complication and the general symptoms are more severe.

The tongue is coated, usually dry, and indented where the edges come in contact with the teeth. The breath is foul and salivation is marked. Herpes labialis is often present. The epigastrium shows distension and tenderness. The vomitus contains HCl with lactic and fatty acids, and mucus, and there is motor insufficiency of a mild degree. The test meal likewise shows evidence of stagnation and perhaps subacidity, while mucus is excessive. After a test breakfast the bread is almost unchanged, much mucus is present, and HCl is absent or much diminished. There is usually constipation or later on diarrhœa, and involvement of the intestines is an important and often troublesome complication. Jaundice may be present if the common duct is obstructed by a plug of mucus. The urine is scanty, high colored, has a high specific gravity, and shows abundance of urates.

**Diagnosis.**—The etiology is an important factor, while the acute onset and the reaction to treatment suffice to make the condition clear. The absence of a known and plausible cause should suggest caution in a diagnosis which may subsequently require modification. The differential diagnosis deals mainly with gastric neuroses, neuralgia, and hyperacidity, hysteria and ulcer. Further, biliary colic, catarrhal jaundice, appendicitis, incarcerated hernia, ileus, and the onset of some infectious disease, especially typhoid fever, scarlet fever, smallpox, and pneumonia have to be considered. The gastric crises of tabes dorsalis, the onset of meningitis in children, and lastly pregnancy should not be forgotten in considering the differential diagnosis, for awkward mistakes are thereby avoided. The appropriate adjustment of the history and symptoms to the physical findings will usually in time make the diagnosis simple. *Exclusion of the important causes of a secondary gastritis* is the essential point.

**Prognosis.**—This depends on whether the condition be primary or secondary, and the gravity of the associated underlying cause. As a rule, primary acute simple gastritis quickly responds to appropriate treatment. The more frequent the attacks, however, the greater the liability to recurrence. The course and duration depend very largely on the cause and severity. The symptoms may last merely for twenty-four hours, or in severe cases for several weeks. Sometimes vomiting relieves at once, but such cases are in most instances merely acute dyspepsia, *i. e.*, acute disturbances of function. When the intestines are involved the disease is aggravated and its duration lengthened.

Fatal cases are those in which the gastritis is secondary to some other disease, usually some severe infection or intoxication.

**Treatment.**—*Prophylaxis.*—In children the cause is more frequently dietetic than in the adult, and in them proper feeding is an important prophylactic measure. The overloading of children's stomachs with unsuitable food is a frequent cause of gastritis.

*The Direct Treatment.*—Two considerations are of special importance: (1) To remove the cause. (2) To protect the stomach and lessen the inflammation.

1. Nature often provides for the removal of the cause by inducing vomiting, and subsequently anorexia; or else emesis may be produced by some simple measures. The remnants often irritate and keep up the symptoms, and are liable to add intestinal disturbances, so that frequently it is well to wash out the stomach; this is especially useful with children because thorough and rapid in its effects. When vomiting is not rapidly induced one may use emetics with care, apomorphine hypodermically, or a mixture of tartar emetic, gr.  $\frac{1}{4}$  (gm. 0.016), and pulv. ipecac, gr. 5 (gm. 0.3), every quarter of an hour until it acts. The latter drug is especially useful for children in the form of vin. ipecac. in 5j doses. Other medicines are rarely required.

2. For twenty-four hours the stomach should be given as complete a rest as possible. A little ice relieves the thirst and a suitable mouth-wash should be in frequent use. Whatever else is given should be in small quantities and only in fluid form, for example, a little weak, unsweetened tea, perhaps with brandy; effervescent water or soda lemonade; peppermint tea; later milk and lime-water (or soda-water) may be taken, other food being begun only when the desire for food returns. Pancreatized milk is also useful. Broths, gruel, and a little stale bread may be added. Solid food is given later on if no diarrhœa be present, the transition period being devoted to light puddings, rice, etc., then lean fish, and later on stewed chicken and fillet. Light vegetables should be allowed only after some days of convalescence when the stools are quite normal, for relapses are common and easily induced by too early a return to a mixed diet. Rectal feeding is rarely needed, but is advisable for those of advanced years.

*Medicinal.*—The early administration of muriatic acid is beneficial, sometimes, as Riegel advises, in 8 to 10 drop doses of the dilute acid in a wineglass of water, taken in sips before meals, or else, as Eichhorst prefers, given after food. Narcotics are not usually required, and may do harm by stopping peristalsis and thus prolonging the symptoms.

*Mechanical Measures.*—A Priessnitz compress and an early warm bath are sometimes of use.

*Special Symptoms.*—For the constipation, drastic purgatives are to be condemned; however, small doses of calomel and soda are useful, especially for infants, or castor oil and laudanum. "Fluid magnesia" is preferable in mild cases because less drastic. For the diarrhœa, lime-water in doses of a few ounces every two hours, or bismuth and chalk in powder form may be given. For the nausea and to rest the stomach,



cocaine in doses of gr.  $\frac{1}{4}$  (gm. 0.016), or creosote in 1 drop doses may benefit. Vomiting is best treated with rest, and the administration of dilute hydrocyanic acid in doses of 5 minims with bismuth, soda, and spirit of chloroform, although, as a rule, a sufficiently prolonged abstinence will in itself suffice.

**Phlegmonous Gastritis.**—**Synonyms.**—Interstitial purulent gastritis; inflammation of the submucosa (Rokitansky); gastritis submucosa (Dittrich, Klebs, and others); phlegmon ventriculi; linitis plastica et suppurativa (Brinton); linitis phlegmoneuse.

**Definition.**—This is an acute suppurative inflammation of the gastric submucosa, sometimes primary, but usually secondary as a metastatic or other infection. It may be diffuse or circumscribed. In 1904, Robson and Moynihan collected 85 cases. Since then others have been described, and more than 100 cases are now on record.

**Etiology.**—The condition is rare, especially in its primary forms, and but few cases are on record. The primary cases are doubtless all microbic in origin, although alcohol is often regarded as a predisposing factor. Such were the cases described by Welch, and E. Janeway and Kinnicutt. Marasmus, faulty diet and ptomaines, corrosive poisons, *e. g.*, oil of turpentine (Kelyack), oxalic acid and trauma of various kinds (Hopkins), all play a part. A fair proportion of cases follow gastro-enterostomy and other operations of the stomach. The commoner causes are some general infection, *e. g.*, scarlet fever, smallpox, typhoid, etc., an ulcerating cancer or infected ulcer, or some defect in the mucosa admitting virulent bacteria. In a number of the cases hemorrhagic erosions suggested the site of invasion, or the infection may occur through the mucous membrane, even without the presence of a defect (Konstantinovitch). More rarely pus swallowed from a suppurative stomatitis has caused the disease. Streptococci have been the commonest microorganisms present, and the colon bacillus frequently coexists. Many other common bacteria have been found and sometimes yeast. But, as Cecil and others have pointed out, the bacteriological examination is not always satisfactory, for coccus forms may die off early, leaving the field to other organisms not directly associated with the true cause.

**Age.**—The youngest patient afflicted was ten years of age (Hun), the eldest eighty-five. The diffuse lesions nearly all occurred between twenty and sixty years.

**Sex.**—The proportion is about four males to one female.

**Pathology.**—Of the 96 cases collected, 76 were probably of the diffuse variety and 12 were definitely circumscribed. The remaining cases recovered or did not come to autopsy. The disease commences in the submucosa, and unless a local ulceration (benign or malignant) exists, or some generalized infection, it is not always easy to determine the origin. Cases originating in chronic ulcer and in cancer are not uncommon. The submucosa, especially at the pylorus, is thickened, infiltrated with pus or sero-pus, sometimes almost jelly-like or œdematous in appearance. The underlying muscle is involved to a greater or less extent; indeed, it may be entirely destroyed. Sometimes merely a channel or cavity remains, containing little or no pus whatsoever. The

mucosa is usually more or less affected and signs of infiltration are seen between the glandular loops.

The mucosa itself is also thickened, hyperemic, and ecchymotic in patches. The epithelium is here and there degenerated, and erosions and ulcers are frequent. Sometimes the sinuses leading from the submucosa are so numerous as to give to the lining membrane a coarse or fine sieve-like appearance, as in a case described by Polak. The result may be that more or less of the mucosa itself is lifted away from the underlying submucous layer. The peritoneal surface shows at times marked swelling of the lymphatics. Perigastritis always accompanies the malady and adhesions occur in various ways and situations about the viscus. Purulent peritonitis is not an infrequent termination, or infiltration and dissection may occur along the submucosa of the duodenum or up into the œsophagus (Chvostek). In some instances the diaphragm has been invaded, resulting in a purulent pleurisy or pericarditis. Thrombi are often found in the neighboring veins and the causative microorganism is not infrequently detected in the vessels.

Splenic tumor, acute nephritis, necrosis of the colon, mediastinitis, cholecystitis, etc., may result from the primary gastric affection, or as a part of a general septic state. The circumscribed phlegmonous gastritis forms an abscess of varying size in the submucosa, or there may be numerous smaller collections. Perforation may occur into the stomach cavity, externally into the peritoneum or into neighboring viscera.

**Symptoms.**—*The Diffuse Variety.*—The onset is nearly always sudden, although with no characteristic symptoms. A rigor may usher in the affection, followed by a rise of temperature to 104° or 105° F. There is general malaise, and severe prostration appears very early. Very soon the gastric symptoms become marked. Not infrequently two stages are evident, at first the signs of gastritis and later those of peritoneal inflammation. Some cases, however, show no gastric symptoms whatever, and the condition is found only after death.

*Nausea* and *vomiting* appear early, are of long duration and rarely, absent. Toward the end the vomiting usually diminishes; it may be feculent and foul in odor. The vomitus rarely contains macroscopic pus (as in the cases described by Glax, Deininger, and others), unless the mucosa be perforated, although leukocytes are usually seen on microscopic examination of the gastric contents. Progressively increasing pain in the epigastrium is a prominent feature and rarely absent. Soon the pain extends over the whole gastric area, resembling that of local or general peritonitis. Tenderness is usually present, and if a large abscess exists fluctuation may be detected. Meteorism is often marked. The fever is irregular, usually persistent, and has a wide range; in Testi's case, however, there was no elevation of temperature. Repeated rigors are sometimes present. The pulse is rapid, small, and often irregular in volume and rhythm. There may be diarrhœa or constipation, and thirst is often marked. Collapse, which has been imminent from the onset, becomes progressive; delirium and coma usually usher in the final stage, with or without the signs of general peritonitis. The *course* is pro-

gressively downward and the duration is rarely longer than two weeks. The diffuse cases are more rapid than those which are circumscribed.

The *circumscribed variety* presents a similar type of symptoms, although at first less severe. Sometimes pain is quite absent. A distinct tumor is often felt. The abscess may burst into the peritoneal cavity and cause death, or rupture may occur through the mucosa into the stomach. Some of these cases recover as pathological specimens testify.

**Diagnosis.**—This has rarely been made. The signs are those of acute peritonitis (local or general). Leube has pointed out that the vomiting of pus need not be pathognomonic, and may arise from a purulent gastritis alone. The probable diagnosis is suggested when in the course of a pyemia or other severe general infection, the symptoms arise as above described, although this form of metastatic infection is comparatively rare. The circumscribed form is perhaps more readily diagnosed, especially when a tumor, which has already been felt, disappears after the vomiting of pus; though this may arise from an abscess arising outside of the stomach and perforating into the viscus. Leukocytosis is probably present in most of the cases (Lengeman). In the differential diagnosis one must consider chiefly perigastritis following ulcer, peritonitis, acute pancreatitis, cholecystitis, abscess of the liver, and corrosive poisoning.

**Prognosis.**—About 95 per cent. of the recorded cases have been fatal. Death usually occurs within one week, and many end fatally in two or three days. The more subacute and chronic cases later on develop peritonitis or metastases.

**Treatment.**—This is symptomatic, unless a localized abscess is diagnosed, in which case operation offers some hope of success. Mikulicz had a patient thus cured (Lengeman). Bovée recently described an undoubted phlegmonous gastritis cured by gastrostomy and drainage.

**Severe Toxic Gastritis.**—Various irritant and corrosive poisons when brought into contact with the gastric mucosa induce an intense inflammation which is merely an aggravated form of the acute simple gastritis, the intensity depending on the character of the poison, its nature, concentration, quantity, and length of time present in the stomach, as well as upon the volitional or accidental ingestion of the irritant. These cases are not necessarily severe, and all stages occur from simple hyperemia to ulceration, gangrene, and perforation. Practically all the known poisons may directly or indirectly induce a severe gastritis.

The *exogenous* poisons are especially irritant in their action, *i. e.*, concentrated acids, alkalis and alkaline salts (sodium and potassium salts, potassium and sodium hydrates, ammonia compounds, etc.), metalloids (chlorine, bromine, and iodine preparations, phosphorus, sulphur, arsenic, and antimony), metallic salts (lead, silver, zinc, copper, mercury, etc.), certain of the methane derivatives in large doses (alcohol, petroleum, croton oil, etc.), bodies from the aromatic groups in certain dosages (benzol and its derivatives), ethereal oils, turpentine, balsams; also some of the alkaloids and glucosides, etc.

The *endogenous* group includes poisons which are supposed to result from retention in the body of injurious substances which are under normal conditions eliminated by various channels, *e. g.*, in uremia and



cholemia, and also poisons resulting directly from metabolic disturbances of a profound nature (diabetes, carcinoma, etc.). Further, there are the bacterial products from all forms of infections, almost any of which may directly or indirectly act as irritants to the gastric mucosa.

The action of the different poisons varies not only according to their nature, but likewise according to the method of ingestion and the position of the victim while taking the irritant. The site of the lesion varies. Sometimes but a small portion is affected; sometimes merely the cardia is involved; or, again, only the greater curvature. Most change naturally occurs where the poison was longest in contact with the wall, which event occurs in most instances at the fundus, pylorus, and posterior wall. As repair takes place, scars form, and according to the extent of the original lesion mere cicatrices exist, or else more or less deformity develops. As a result one may find pyloric stenosis, hour-glass contractions, sacculations, etc. Often very extensive lesions heal remarkably well. The mucous membrane is not impaired. The secretory changes are marked; hydrochloric acid diminishes or is completely absent.

As a rule, the alkalis are more penetrating than acids; perforation is extremely common, and where the serious effects are not fatal one usually finds more or less deformity of the œsophagus as the result of cicatricial contractions. Often the œsophagus alone is severely affected, for the acid becomes diluted in its journey to the stomach.

**Symptoms.**—In a typical case the sudden severe onset of pain and vomiting is the most prominent feature. The pain is usually felt all the way from the oral cavity to the stomach. There are burning pains in the mouth and gullet, and behind the sternum. Nausea, retching, and vomiting follow almost immediately. The vomiting is frequent, painful, and brings no relief of the symptoms. In the vomitus blood-stained material, perhaps food remnants, mucus, shreds of mucous membrane and the poison itself are found. Great thirst is a prominent symptom, and the dysphagia intensifies the suffering. Diarrhœa appears later, and the stools may show evidences of mucus and blood, usually because of an accompanying enteritis. Signs of collapse rapidly supervene. The facies is anxious and pale, or cyanosed, and the lips and mouth show evidences of the corroding poison. Petechiæ often appear in the skin, and jaundice is not infrequently present from toxic or obstructive causes. The pulse is rapid, small, and often irregular in volume and rhythm. The respirations are shallow, quickened, and thoracic in type, because the diaphragmatic movements are limited through the pain. The temperature may rise slightly above the normal. The condition of the sensorium varies according to the exciting cause. In many instances there is great excitement, convulsions intervene, and, later on, coma.

The condition of the *urine* depends on the kind of poison ingested. The abdomen in the acute stages shows nothing beyond tenderness and distension, unless perforation and peritonitis have occurred with their usual signs. Death occurs usually from exhaustion, convulsions, suffocation, or from general intoxication. Should recovery take place, complete restoration of the tissues may occur in those cases where no marked corrosion of the gastric mucosa has been present, but this is only

with the milder forms of irritant poisoning. In other cases the results are less favorable. Chronic indigestion supervenes from atrophy of the glands, or persisting gastritis with vomiting, progressive weakness, and emaciation. Sometimes ulcerations persist, or their healing results in the formation of stenoses and deformities.

**Diagnosis.**—This is based on the history, the nature of the symptoms, the oral and pharyngeal evidences of corrosion, etc., the odor of the breath in certain cases, the chemical analysis of the vomitus or of the washings from the stomach, and the analysis of the urine.

**Prognosis.**—This depends upon the special cause, the kind of poison, its amount in relation to its toxicity and irritant properties, the early emesis, and the possibility of early removal. Collapse and peritonitis are serious symptoms.

**Treatment.**—Rational therapeutics depend upon a recognition of the special toxic agent, for which the proper antidote can be given. In addition to this, one should attempt to get rid of the poison, if early recognized, by rapidly acting emetics, *e. g.*, apomorphine. Lavage should be used when it is improbable that extensive corrosion is present, and soothing remedies for the gastric mucosa may then be administered. For corrosive acids one may give mucilaginous and oily drinks or weak alkalis. For corrosive alkalis, vinegar and water, or citric acid are useful. Counterirritants externally may aid in giving relief, while medicinally one should use demulcents, opiates, bismuth, etc. Rectal feeding will be necessary for some days. Collapse must be checked, or treated by appropriate remedies.

**Mycotic Gastritis.**—Many of the commoner parasites are found in the stomach under normal or abnormal conditions, both bacteria and mould fungi, as well as yeasts, and while in many instances they are the direct cause of changes in the gastric functions or anatomical conditions, at other times their presence seems to be rather accidental and unimportant. Inflammation of the gastric mucous membrane as a result of bacterial invasion through the blood or lymph streams is common enough, and gastritis due to streptococci, typhoid bacilli, pneumococci, and other infectious agents is well recognized. Whether or not bacteria which are ingested with the food can induce a true gastritis seems still open to question. It would appear that the acid gastric juice retards the growth and development of bacteria, although moulds seem to resist the acid better than do the schizomycetes, which latter grow better when sub-acidity is present. The acidity, the stagnation, and the quality of food ingested are the factors which determine the growth or retardation of development of the various fungi in the stomach.

As a general rule, moulds and yeasts do but little harm in the stomach and have an anatomical rather than a clinical interest and importance. Kunderat found favus in the stomach associated with a favus universalis, which was distributed throughout the body, and Rudnew found the penicillium glaucum in a woman who died of Asiatic cholera. Klebs and Fraenkel associated a gastritis with favus, yeast, and oidium albicans; certainly the last-named fungus has often been seen in cases of gastritis, and yet in spite of its frequency during childhood in the pharynx and

œsophagus, it is rare in the stomach. Epstein drew attention to the fact that a healthy mucosa was not a suitable medium for the growth of this parasite in the pharynx, and perhaps the same applies to its growth in the stomach. This may account for the frequently abrupt termination of the affection at the cardia, despite the fact that large numbers of the fungi reach the interior of the stomach. Reisz described the stomach of a girl aged eighteen years which was covered with patches of fungus growth, the underlying epithelium was partially degenerated, and the mucosa infiltrated with small round cells.

Von Wahl and von Recklinghausen recorded cases in which fungi of the leptothrix group penetrated the gland ducts and were anatomically associated with necrotic areas. In one case many pustules existed in the glandular layer and submucosa of the pylorus, in the other the fundus was chiefly involved.

**Symptoms.**—The relation of the presence of moulds to the symptoms is dubious. Talma was of the opinion that the carbohydrate fermentation, caused by the presence of microorganisms, was the antecedent of many cases of hyperacidity, but although moulds may coexist with hyperacidity and gastralgia, it is not certain whether their presence is a cause or an effect of the condition found. Einhorn has admirably described a few cases, and was among the first to recognize the condition clinically. The lavage water from the empty stomach demonstrated the presence of blackish-gray or brownish-green flakes indicating the existence of moulds which microscopically showed spores and mycelia. The species could not be determined even though carefully examined. These flakes varied in number from 4 to 50 or more, were 2 to 5 mm. in size, and often intimately mixed with mucus, which fact together with their presence in the empty stomach argues that their presence is not merely an accidental admixture. Probably the moulds adhered closely to the mucous membrane and perhaps proliferated in it. At all events they can evidently thrive in the stomach and retain their power of growth, regardless of the gastric juice.

Two types of cases occur, one with signs of hyperchlorhydria (occasionally with hypersecretion and vomiting), the other with gastralgia, the gastric secretion being normal or reduced. The relation of the fungi to the symptoms is either etiological or a cause of increased severity. Lavage improves the symptoms.

**Treatment.**—Systematic lavage rapidly removes the fungi permanently from the stomach. Einhorn advised the further use of weak solutions of silver nitrate in the lavage water.

**Diphtheritic Gastritis (Gastritis Membranacea).**—This condition, which has much more anatomical than clinical significance, may be defined as a pseudomembranous inflammation of the gastric mucosa, usually a sequel to a similar condition of the nasopharynx, but sometimes primary (Delafield) and associated with varying bacterial agents, and at other times apparently due chiefly to chemical causes.

True *diphtheria* of the stomach, due to the Klebs-Loeffler bacillus, is a rare condition and nearly always secondary to a similar bacterial invasion of the contiguous parts, œsophagus, throat, or upper respiratory passages.



Leary observed only two instances out of 136 fatal diphtheria cases examined at the Boston City Hospital. While, as a rule, diphtheritic gastritis is secondary to some other diphtherial infection, it may complicate various other infectious diseases, *e. g.*, typhoid fever (Thorel), pneumonia (Foulerton), pyemia, the exanthemata, etc. Isolated instances of the malady were described by Sir William Jenner, Wilson Fox, Wilks, and others. Children seem to be most commonly affected.

**Pathology.**—The stomach is not usually altered in size or shape. The chief feature is the presence of the pseudomembrane. This may be diffuse and cover the entire surface of the stomach as in the case described by Talfourd Jones, but more often there are streaks or patches of membrane—of varying size, thickness, and number, irregularly arranged. The mucosa is discolored, usually darker than normal, reddish or grayish red in appearance, and thickened. The rugæ are usually well-marked, and covered with the more or less firmly adherent membrane. Microscopically the picture resembles that seen in ordinary pseudomembranous lesions of any mucous membrane. As in pseudomembranous inflammations elsewhere, so here the bacteriological findings vary widely. Streptococci and Klebs-Loeffler bacilli are those most commonly isolated.

**Symptoms.**—There are no characteristic symptoms, and the mere vomiting of a pseudomembrane does not necessarily imply that the disease has affected the stomach itself—unless, indeed, a cast of the whole stomach be vomited up, as was recorded by Thomson in one instance. Such membranes are readily swallowed and sometimes are so extensive as to cause pyloric obstruction. Seitz, however, has recorded a diagnosis of pseudomembranous gastritis during life and confirmed at autopsy. Some of the membrane has been vomited concurrently with the presence of other evidences of gastric disturbance.

## CHRONIC GASTRITIS

**Definition.**—A protracted inflammation of the gastric mucous membrane with motor or secretory changes in gastric digestion. It may be primary or secondary.

**Incidence.**—In its primary pure form the condition is clinically quite uncommon—at all events much more rare than is ordinarily supposed—being frequently confused with a purely functional disease in which similar signs and symptoms exist without any pathological changes. For this reason, and in view of the unsatisfactory means of diagnosis, the time-honored term “chronic dyspepsia” should not be despised. It may be that after some time even functional disturbances lead to pathological changes in the gastric mucous membrane, a true superficial inflammation, as in the cases referred to by Cohnheim, in which the gastritis resulted in his opinion from motor insufficiency, and was induced by irritation of the stagnant chyme.

As a primary affection, chronic gastritis is not often found in the autopsy room, the cause of death usually being some general or local condition to which the gastritis is secondary (cardiac or hepatic disease,

nephritis, tuberculosis, pernicious anemia, etc.). Thus, in the Royal Victoria Hospital, among 1300 autopsies, there were 108 with chronic gastritis, and of these, 92 were definitely secondary to other causes, while the remaining 16 were more or less mild in type and associated with other diseases not necessarily the cause of the condition. Statistics, however, with reference to the incidence of chronic gastritis are notoriously unreliable. *Clinically*, the signs and symptoms are often most ill-defined as evidence of true inflammation of the stomach, and much has been called gastritis which undoubtedly would more truly come under the category of neurosis of the stomach, or under the old name of chronic dyspepsia, a purely functional disorder often due to atony. *Vice versa*, many cases of chronic gastritis as seen at autopsy (secondary to other diseases) were utterly devoid of evidence of that malady during life.

Pathologically, statistics are almost equally unreliable, through the infrequency with which primary gastritis comes to the pathologist's notice, and because of the numerous errors in pathological observations. Marked contractions of the gastric wall are mistaken for chronic thickening, and passive congestion for true gastritis, where a microscopic examination would have revealed no sign of disease.

**Classification.**—Classifications have been based upon the nature of secretions, and the gastritis *acida*, gastritis *anacida*, gastritis *mucosa*, etc., have been described. The mere analysis of the secretions, however, affords practically little clue to the underlying conditions, and cannot determine differentiation from certain neuroses. In many instances a hyperacid secretion is found in the early stages of chronic gastritis to be followed later by a diminution of the hydrochloric acid. Sometimes, however, hyperacidity may appear late, while not infrequently it persists throughout the whole course. When one realizes how widely the secretions may vary from day to day; how on one day an excessive acidity may be followed by a marked hypochlorhydria on the next; how intermittent is the pathological secretion of mucus, one can scarcely feel safe in relying upon a classification of chronic gastritis based on such clinical signs. As well might one classify the various forms of pneumonia according to the account and character of the sputum.

The term *mucous gastritis*, for example, is used to designate the simple chronic gastritis, or gastric catarrh, in spite of the fact that mucus may be abundant in any of the different pathological varieties of this malady. Again, in hyperacid gastritis much or little mucus may be present, and the underlying condition may be proliferative and degenerative in nature. Proliferative gastritis, as a rule, induces diminution in the secretion of HCl, although, in many instances, there is hyperacidity. In cases of chronic gastritis with atrophy of the glands (*anadenia*, *achylia gastrica*), the symptoms and signs are apt to be most constant; in certain instances of this variety there is a rapid course with signs of chronic gastritis and progressively downward tendency. Examination of the gastric contents after a test meal shows little or no digestion and the secretions appear absent. Here, however, as in the other forms of chronic gastritis, great variations occur in the symptoms at times, and,

moreover, there are all grades of transition to the other varieties of the disease. Again, whether owing to treatment or to the natural course of the malady, a hyperacid gastritis may change to the anacid type, and, *vice versa*; if enough gland elements remain, the condition of achylia gastrica may alter to one with normal or even hyperacid secretion.

Apparently the state of the *motor* power has greater significance in the production of clinical signs and symptoms than has the secretory function; often indeed the marked evidences of the malady are synchronous with the signs of motor insufficiency. Certainly many cases in which autopsy has shown marked disease of the gastric mucosa have given few symptoms during life so long as the motor power was unimpaired. It would seem well, therefore, to avoid any clinical classification into subdivisions, and to recognize the fact that the manifestations being varied, one may recognize the malady from the complexity of signs, symptoms, etiological factors, and be content with the general diagnosis in all such cases of "chronic gastritis."

**Etiology.**—Primary chronic gastritis is mainly caused by irritants acting over a prolonged period and in a strength not so great as to corrode the mucosa. Oft-recurring acute gastritis is followed by the chronic form. Alcohol is the commonest irritant, and the most important cause, especially if taken undiluted, *e. g.*, brandy, gin, or wines of all kinds when taken to excess—their action being either as direct irritants or perhaps in part due to the production of acids in the stomach. So also diluted alcohol may act in the same way by inducing acetic fermentation.

An analysis of cases in the Royal Victoria Hospital has called our attention to the fact that alcohol in excess is by no means a necessary cause. In 10 autopsies performed on men dead of acute alcoholism, 7 showed no definite chronic gastritis whatever, while in the others the signs were marked in only one. Of the autopsies upon 40 other patients, in whom a marked alcoholic history was obtained, but in whom death was due to other causes, there were 20 cases with chronic gastritis, and the remainder showed no definite signs of true inflammation; 10 showed mere congestion, 10 showed swelling and congestion, 9 showed a granular mucosa, and only 5 showed definite thickening; 4 others had mammillations, and in the remaining 2 true polypi existed. Macroscopic erosions existed in only 1 of these 40 cases. It is interesting to note that 21 of these 40 patients gave no history of gastric symptoms, while 16 had pain and vomiting.

Other causes of irritation acting directly or indirectly are spices, strong tea or coffee, certain irritant drugs and drastic purgatives, as also tobacco, especially if chewed, and dietetic errors, Improper quality of food (if coarse, too rich, too spicy, fatty, or otherwise irritating), excessive quantity as regards bulk, especially of rich foods, improper mastication of food and also irregularity at meals are all of great importance, and more so in proportion as the individual's habits are sedentary.

*Secondary gastritis* may be due to local or general conditions. The chief local conditions are as follows: Gastric diseases of any chronic nature, affections of the portal system, especially obstruction, and also the presence of parasites (bothriocephalus, etc.). The main general



conditions are numerous, *e. g.*, cardiac and arterial disease, pernicious anemia, leukemia, gout, diabetes, etc., and general infections (typhoid fever, pneumonia, tuberculosis, sepsis, etc.).

**Pathology.**—Pathologically two main types of chronic gastritis exist, the one *chronic productive*, the other *atrophic*. In the productive type, part or all of the stomach wall is thickened, while in the atrophic variety it is thinned in one or all of its coats. The stomach is usually larger than normal, except in the cirrhotic forms where there is shrinkage of the organ. At autopsy, mucus is usually thick, or a more or less grayish or slaty color, and sometimes reddened with blood pigment. It is either translucent or opaque, and sometimes appears semipurulent.

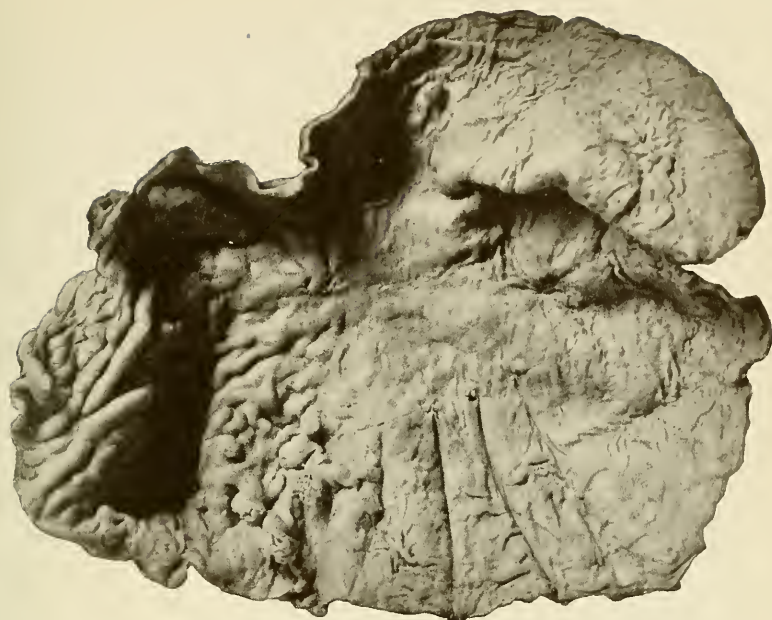
The mucous membrane varies according to the type of gastritis present, but both types may be found in different portions of the same stomach. In the *productive variety* the mucosa is swollen and thickened, and of a dark red or grayish-red color, especially in the neighborhood of the pylorus. The color varies. In the older cases there is more pigment, which appears beneath the mucosa as a black or dark gray discrete discoloration. Not infrequently one sees small, follicular ulcers or hemorrhagic erosions, apparently due to inflammatory hyperplasia of the lymph follicles, with subsequent degeneration. The affection of the mucosa is either general or local. In diffuse inflammation there is dense thickening from interglandular inflammation as well as from productive inflammation of the gland structures. The thickened wrinkled mucosa with its flat mammillated appearance may be polypoid in appearance ("gastritis polyposa") or more coarsely granular (gastritis granulosa). The submucosa and muscularis may also be affected, the muscle itself thickened, and the interstitial tissue increased. One may even see the serosa involved.

*Microscopically*, the mucous membrane shows small-celled infiltration, degenerated epithelium, hemorrhages, cystic dilatation of the gland tubules, and here and there some true erosions. The round-celled infiltration occurs early, is usually chiefly superficial and beneath the uppermost layers of epithelium, as also to some extent between the glands. Small round-celled infiltration may persist for a long period of time without developing into fibrosis. The degeneration of epithelium affects mainly the secreting cells, while the mucous cells appear to resist the inflammation longest. Often the epithelium is so distorted that it is impossible to distinguish chief from parietal cells, and many assume a cylindrical or a cuboidal shape. Cystic dilatation of the tubules is common (retention cysts). This so-called "gastritis cystica" is sometimes very pronounced. Capillaries and lymphatics are usually dilated and there are hemorrhages, old and new.

*Atrophic Type.*—The second type of chronic gastritis, with atrophy of the mucous membrane, sometimes called *anadenia ventriculi*, is said to be preceded usually by gastritis proliferans. The mucous membrane is devoid of properly developed glands. The surface is pale, thin, and smooth and in the advanced cases consists more of granulation tissue or well-developed fibrous tissue. The muscularis takes part in the process and is usually atrophic. Sometimes, however, there is

# PLATE VIII

FIG. 1



Chronic Productive Gastritis.

FIG. 2



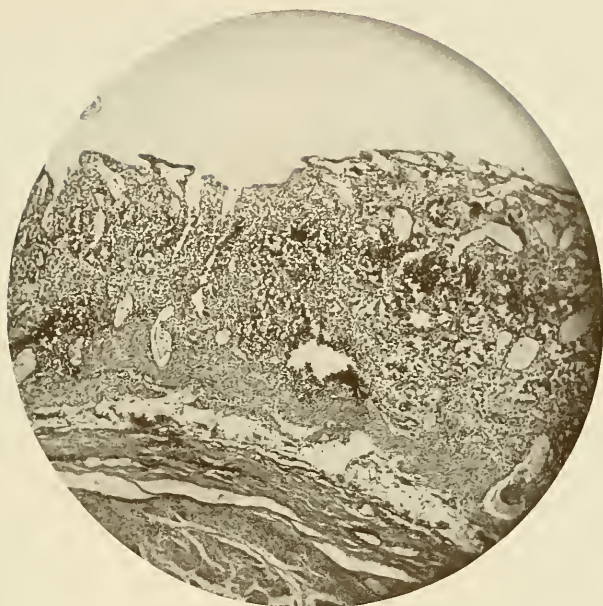
Chronic Productive Gastritis.





PLATE IX

FIG. 1



Chronic Productive Gastritis.

FIG. 2



Chronic Atrophic Gastritis.



muscular hypertrophy with atrophy of the mucosa, and one may see pigmentary changes, the so-called atrophic pigment induration of the stomach.

Microscopically, the mucosa resembles more and more that of the small intestine. There are evidences of round-celled infiltration. The atrophy of gland structures varies; often the secreting glands are alone involved, while the mucoid cells are unaffected; but the changes in this respect vary in different cases, as well as in different portions of the stomach in each individual instance. Illustrative types of these cases are often found in pernicious anemia. Some advanced cases are difficult to distinguish from a diffuse scirrhus, the gland structures being so atrophied that only a flat fibroid-looking surface remains whose base enclosed the remains of gland structures.

*Cirrhosis of the stomach* is only another variety of the atrophic in the sense that gland structures disappear. Here the organ is smaller than normal, contracted, and thickened usually in all its coats from excessive growth of the products of chronic inflammation.

**Symptoms.**—The disease both in its primary and secondary forms, may be latent throughout, or gradual and insidious in onset. To a certain extent the symptoms and signs depend upon the condition of the secretions and motor power (sthenic and asthenic, hypertrophic, sclerosing or atrophic), although certain general features apply to most of the cases.

Early symptoms are usually those of a so-called dyspepsia; slight dietetic errors cause discomfort in the epigastrium, with a sense of fulness, pressure, or weight, and perhaps even slight pain. Unless hyperacidity exists there is usually anorexia, especially for meats, or the appetite is fickle, with yearning for spices, acids, or liquids. A disagreeable taste in the mouth is present, and flatulence commonly intervenes, often being a marked symptom. Eructations of gas frequently relieve the distress. The tongue may be furred and is often sore at the edges and tip. Nausea and vomiting occur either at the height of digestion or sometimes in the early morning—perhaps induced by the swallowing of pharyngeal mucus during the sleep. Thirst is usually present, although less common than in acute cases. Lassitude, neurasthenia, and dizziness during the digestive period are the rule. Later in the disease, when the condition is more pronounced the symptoms are aggravated. Nausea is more persistent, waterbrash and cardialgia are more common, and vomiting comes on with greater frequency and the vomitus contains undigested food with fermentation products. Fluids may be well borne, but solids aggravate the symptoms. The *intestines* are likewise affected, and constipation alternates with diarrhœa. The *nutrition* varies. Emaciation may be rapid when the intestinal functions are simultaneously impaired. The urine shows urates and calcium oxalate is often present in excess. Not infrequently the ethereal sulphates are increased.

Physical examination of the abdomen gives little information, as the only constant sign is tenderness—more or less diffuse and perhaps more often found to the right of the epigastrium than elsewhere. The stomach may or may not be distended.



**Gastric Contents.**—Usually the food removed is abnormally large in amount, appears undigested, coarse, and mixed with mucus. The most constant abnormality is the excessive amount of *mucus*, although it may originate in some portion of the tract above the stomach, *e. g.*, pharynx or œsophagus, and need not be an evidence of disturbed gastric function. Mucus from the stomach occurs more commonly in shreds or flakes, not in isolated lumps, is mixed with the food and is often found in most abundance after the test meal has been removed and the remaining contents gained by thorough lavage. It usually contains leukocytes in more or less abundance. The presence of abundant gastric mucus enclosing many leukocytes is positive evidence of gastric catarrh.

*The secretion of acid* varies. Best and Cohnheim showed that in gastritis we first have subacidity through deficient secretory function and the neutralizing effect of alkaline mucus. The gastric juice is thus too weak to exercise its inhibitory acid action, so that the stomach empties itself too quickly and as a result we again get hyperacidity with its characteristic symptoms. They produced hyperacidity in dogs by artificially emptying the stomach more quickly, *e. g.*, by a fistula, thus doing away with the acid which regulates the movements. *Hyperacidity* is uncommon and when present usually indicates an early condition of the gastritis, or an associated neurosis (gastritis acidæ). Diminution of hydrochloric acid is more common and may be progressive up to the period of total achylia (achylia gastrica, atrophic gastritis). From time to time, however, during the course the amount of acid shows great variation. McCaskey, in an analysis of 600 cases of so-called chronic gastritis, found no hydrochloric acid in 20 per cent., subacidity in 26 per cent, normal acidity in 34 per cent., and hyperacidity in 20 per cent.

The *pepsin* keeps pace with the hydrochloric acid, and the *rennet ferment* likewise diminishes with the progress of the disease. Bouveret regards a quantitative estimation of the rennet ferment as a valuable aid in prognosis as indicating possibilities of repair.

*Achylia* not infrequently occurs in the late stages of chronic gastritis. From the pathological standpoint achylia does not imply anadenia. Faber, especially, draws attention to the fact that in gastritis there may be achylia even although secreting cells are unimpaired, and concludes that the accompanying gastritis has merely disturbed their function but not their anatomical structure. In order to prove that the achylia is not merely temporary, several test meals should be given. The enzymes are absent as well as the hydrochloric acid; mucus may be abundant.

*The motor power* varies. As a rule it is not greatly impaired, although if insufficiency be present there is much more fermentation and the general gastric symptoms are much more pronounced. In most cases of typical chronic gastritis there is some atony, more readily induced by persistent dietetic errors. The gastric functions are readily taken on by the intestines when normal motor power exists. Gastrectasis is uncommon.

Some authors (Cohnheim and others) described valuable aid from examination of bits of *mucous membrane* which sometimes come away

with the lavage water, but Lubarsch's studies have revealed many sources of error in this means of diagnosis. The alterations they present are often but semblances of inflammatory change; and *vice versa*, even if the cells and glands be actually altered structurally, it does not necessarily mean that they have been functionally inactive. Bassler has directed attention to the value of free gastric cells in the fasting stomach as evidence of the atrophic variety. Saline installations are used (250 cc. of water with sodium chloride 21 grs., sodium sulphate, sodium carbonate and sodium phosphate  $\bar{a}\bar{a}$  1 grain). The fluid is drunk, the stomach agitated by palpation and exercise, and after five minutes the fluid is siphoned off and allowed to stand. The sediment is then examined and the cells are differentiated by eosin (for acid cells), and hematoxylin (for peptic cells). In atrophic gastritis the acid cells are in abundance and stain readily, with stippled protoplasm and eosinophile granules with well defined nucleus.

**Course and Prognosis.**—It is usually of long duration, and the general health suffers either periodically or progressively, but alternation of good and depressed health is the rule. The mental condition suffers, neuroses appear and often great physical depression as a result of the hypochondriasis and neurasthenia. The exacerbations usually depend on indiscretions, and recurrences are very common, especially in alcoholics. The mild cases are readily cured, but in the more severe ones the probability of cure depends on the condition of the muscular wall, the state of the mucosa, and the kind and degree of inflammation present. With atony of the stomach, and especially gastrectasis, and with achylia gastrica, the condition is much more difficult to treat successfully. When the intestines are healthy, the chances of cure are naturally augmented. The prognosis should be based less upon the general condition than upon the outlook for securing a sufficient supply of nourishing food and the maintenance of secretory and motor functions. In every case the individual affected has himself most to do with the cure by observing due regard to the requirements of treatment, which, after all, are readily followed and are usually of benefit in cases not too far advanced.

**Diagnosis.**—The condition whether primary or secondary is very often latent, and repeated observations may be necessary; the etiology, the symptoms and signs as above described render the diagnosis certain, but by *exclusion* rather than by any other means. The main features in the diagnosis are: (1) The etiological factors. (2) Persistent indigestion, with nausea and frequent vomiting of much mucus, gastric pain, and tenderness. (3) The relation of the symptoms to the ingestion of food. (4) The variations in the course, with its exacerbations and remissions. (5) The moderate loss of strength and weight as compared to the lowered nutrition in more serious conditions. (6) The comparatively slight alterations of the motor power. (7) The presence in the gastric secretions of much mucus and variable quantities of acid from complete achylia to hyperacidity. (8) The finding in the stomach contents of many leukocytes either in the mucus or in bits of mucous membrane. (9) The beneficial effect of proper treatment.

In the *differential diagnosis* one must distinguish between primary and

secondary forms; the primary affection is much more uncommon than the secondary, hence the importance of detecting the original cause.

*Chronic Gastritis and Gastric Neuroses.*—The differentiation is often impossible. The distinctive features are as follows: In chronic gastritis, (1) An obvious cause. (2) Poor nutrition. (3) The symptoms are digestive in time and cause—much mucus is vomited. (4) Gastric analysis. (5) Duration with exacerbations and remissions.

In *cancer* there is no apparent cause, the disease is progressive with wasting, gastric pain, and hematemesis. The gastric analysis differs. There is occult blood in the stools, and tumor may ultimately appear. Treatment has less marked benefit. Atrophy of the gastric follicles, *achylia gastrica*, is an occasional sequel of chronic gastritis, as also an accompaniment of gastric cancer, pernicious anemia, etc. It may, however, occur as a neurosis. Thus, Ewald, Einhorn, and others have found that for years there may be complete absence of hydrochloric acid in the gastric secretions in individuals who are either quite well or merely neurotic. These patients show no dyspeptic signs in spite of the secretory deficiency, and, moreover, show a mucosa which is perfectly normal according to observations made upon bits of mucosa removed in washings. In many instances even after years of *achylia* the secretions may return to the normal. The presence of much mucus and many leukocytes in the gastric contents in cases of *achylia* would seem to favor the diagnosis of gastritis, implying, as it does, a probable catarrh.

**Treatment.**—A detailed diagnosis is essential to the proper treatment of chronic gastritis. *Secondary* gastritis must be treated according to the cause, which will involve the therapeutics of the lungs, heart, liver, or general constitution. In the *primary* cases, on the other hand, the treatment embraces prophylaxis, palliative, and curative measures. The curative measures are mechanical, dietetic, and medicinal. One must consider the cause of the disease as well as the condition of the secretory and motor functions.

**Prophylaxis.**—This is of importance, and one should, therefore, remove any external conditions which tend to bring on or aggravate the malady. Excesses of all kinds must be guarded against; bad habits cured; the patient should be taught to eat slowly, to chew his food well, and carefully to select his diet both as regards quantity and quality. Faulty teeth, an important factor in the etiology of gastritis, should be repaired.

The *mechanical treatment* consists mainly in lavage, and is to be used only when atony and fermentation exist. It is well to clean the stomach before any food enters, to remove any mucus which covers up the superficial epithelium, and prevents proper action of the digestive juices. Lavage may be carried out daily or every second day, in the early morning, or, in severe cases, six hours after dinner (which is usually taken at midday), and the evening meal should be as light as possible. Lukewarm water usually suffices, but if much mucus is present, sodium chloride may be added, or, if there be much fermentation, boracic acid. The lavage water must return clear before the treatment is completed. When, for one reason or another, lavage is impossible, one may employ “natural lavage” by means of frequent administration of mineral waters,



especially the saline waters with carbonic acid, which are often beneficial in relieving the stomach of its mucus and inducing a combination of the organic acids. The alkaline sulphates (Carlsbad) are useful for this purpose as well as for relieving constipation. When there is irritation in the stomach with diarrhœa, they are best taken hot. Whenever atony exists only small quantities of fluid should be taken at one time.

Daily cold baths or shower baths, with subsequent friction of the skin, are of great benefit. When pain or great discomfort is present, a wet compress may be placed upon the epigastric area and covered with gutta-percha tissue. A suitable abdominal binder of thin wool is often soothing to patients who go about, and is a protection to the sensitive abdomen. Electricity is of doubtful value, but the proper regulation of rest and exercise (which latter should always be moderate) is of the greatest importance.

A change of scene, climate, and general surroundings is one of the most efficacious forms of treatment, both for its stimulating effect on the constitution generally, and more particularly as an aid in dispelling the accompanying neurasthenia. A sojourn at some of the numerous watering places is often of the greatest benefit, not so much on account of the waters taken (although they have their definite use), but on account of the diet and general regime under which patients are placed, and under conditions which are not usually followed at home. When this is impossible, suitable exercise and properly regulated diversion are commendable, especially if accompanied by the regular use of mineral waters selected according to the condition of the secretions.

*Dietetic treatment* is of prime importance, although often hard to regulate because of the individual preference. The food must be non-irritating and easily digested, calling for little effort on the part of the gastric juice or muscular action of the organ. When only the scantiest diet is tolerated, milk, preferably diluted with lime-water, may be given at regular intervals, and this, while the patient is at rest, may suffice. Later on a mixed diet, selected with reference to the needs of each case, is advisable. The motor power is the best guide and when this of the stomach is normal, one may administer albumins, starches, and fats. When, again, the secretory power of the stomach is defective, a mixed diet is very easily given, so long as the motor power remains unimpaired. In all cases, however, albuminous food should be finely divided. Carbohydrates should form the bulk of the food in those cases in which the hydrochloric acid is deficient, using preferably those in which there is least residue after digestion is complete.

*Fats* are imperative when malnutrition exists, and for these cases butter and cream form the most easily digested varieties. It is thus essential, when possible, to give a mixed diet, non-irritating, finely divided, and containing as much nutriment as possible within the smallest compass. In severe cases, in addition to the milk, one may give gruel, milk soups, light puddings, rice arrowroot, toast, and then eggs. In some cases minced meats may be added; but it is not wise to add spices or any rich sauce. The craving which many patients with a chronic gastritis have for spicy things, under the impression that they will

stimulate the functions of secretion, should not be encouraged. Of the lighter meats, calves' brains, sweetbreads, chicken, fish, minced beef, are best. Alcohol is to be avoided unless in the form of very light wine. The quantity of water taken with the meals should be restricted, unless there be hyperacidity, in which case it is well to dilute the food moderately. Effervescing alkaline waters may be tried with benefit.

The determination of the proper number of meals per day is based upon the condition of the motor power. If this be good, three meals a day may suffice, but if there be atony, four or five meals, each small in quantity, are better. Weak coffee, tea, and cocoa may be given except in hyperacidity. As the patient improves, such vegetables as spinach, carrots, maize, potatoes (mashed), and macaroni may be added in small quantities and gradually. Bread should be stale and not hot. When constipation is marked, it may be well to give stewed fruits.

*Medicinal.*—Inasmuch as hydrochloric acid is deficient in many cases, one may add a few drops after each meal with benefit. Thirty drops of dilute hydrochloric acid in a glass of water, to be sipped at intervals for an hour after each meal, may be prescribed. On the scientific basis, there is little to be gained from the use of pepsin, although practically one frequently does find that its employment seems to afford considerable aid to digestion. Pancreatin in doses of fifteen grains is perhaps better, and should be administered with soda, although rationally this should not be prescribed unless there is some evidence of atrophy of the gastric follicles. Papain is also recommended by many. After all, these artificially prepared ferments are realized to be of little use when one considers that the intestines carry on the defective actions of the stomach.

It seems of prime importance, however, to give some stomachic before each meal, and for this purpose one may try either dilute nitromuriatic acid, in doses of  $\mathfrak{M}\times$  to xv (1 cc.), nux vomica, quassia, gentian, or condurango. In many cases the greatest relief from the pain incident to chronic gastritis is a pill consisting of silver nitrate, gr.  $\frac{1}{6}$  (gm. 0.01); opium, gr.  $\frac{1}{4}$  (gm. 0.016), and extract of hyoscyamus, gr.  $\frac{1}{2}$  (gm. 0.03).

When fermentation is an annoyance the diet should be carefully looked into; one may sometimes add thymol, carbolic acid, or creosote to the other modes of treatment. Germain Sée has recently recommended the use of strontium bromide, gr. 30 to 60 (gm. 2 to 4), especially when hyperacidity co-exists with the fermentation. For a distinct pyrosis, bismuth subnitrate and sodium bicarbonate, of each 10 grains (gm. 0.6), combined with 3 to 5 grains (gm. 0.2 to 0.3) of calcined magnesia, will usually afford relief. Small doses of atropine may be added with benefit if the secretion of mucus is excessive. For persistent vomiting, lavage is the most rapid means of giving relief. When this is impracticable, a careful adjustment of the diet, with perhaps the administration of one or other of the usual drugs for that purpose, may be of benefit.

Constipation is one of the greatest annoyances. It is well that the patient should develop great regularity in his habits, going daily to stool at regular hours, whether there be any desire or not. As soon as possible vegetables containing much cellulose should be added to his food, also stewed fruits, especially a combination of figs and prunes;

or in the early morning he should drink cold water or eat a fresh orange; and only in aggravated cases should we resort to either purgatives or enemata. When purgation is necessary, it is a difficult matter to determine what drugs should be employed; only the mildest forms of purgatives should be given, and of these aloes and cascara are probably the most beneficial. The use of Carlsbad salts in the morning is another efficacious means of treatment for aggravated constipation.

### MOTOR INSUFFICIENCY

**Synonym.**—Gastrectasis.

**Definition.**—Gastrectasis is an acute or chronic enlargement of the stomach cavity associated with a relative or absolute diminution of motor power. The condition may be mild (mere atony) or severe (retention) and all transitions may occur. It is a clinical sign rather than a disease *per se*. In the severe variety there is permanent stagnation, *i. e.*, retention. It is a functional disturbance of motor power rather than mere enlargement of the organ. Of the functions of the stomach the motor is by far the most important, and modern methods of investigation confirm this view more and more.

The size and motor power of the stomach are not necessarily correlated. It is an organ whose size is subject to very wide variations in health, and clinical experience and x-rays prove the fact that mere increase in its dimensions does not imply a pathological state of the gastric functions. The stomach may occupy almost twice its normal area in the abdomen, and yet the subsequent examination with the stomach tube reveals no disturbance of its motor function. This is mere megalogastria, a matter of size and not of function.

*Various forms of motor insufficiency exist:* (1) Mere atony of mild degree (the commonest form of dyspepsia). (2) Severe atony (idiopathic dilatation), in which food is retained for a long time. (3) Relative motor insufficiency (obstructive), in which some hindrance at the pylorus, either intragastric (often hypertonic) or extragastric, causes the dilatation. These forms have in common one clinical sign, stagnation of food—other signs and symptoms depend on the severity and associated conditions. Probably the commonest form of gastric indigestion is that due to deficient muscular power—the so-called atonic dyspepsia—a condition of “slight motor insufficiency.”

Atony without obstruction is not always easy to explain. Here again confusion seems to exist in the terminology. The motor power depends on rhythmical contractions of the antrum and action of the pyloric sphincter. The fundus plays a subordinate part, though recently an effort has been made to reestablish its importance. Idiopathic dilatation seems to be quite easily induced. Cannon has shown that intragastric pressure has a marked influence on motility and that some mechanical stretching of the viscus is an efficient stimulus to muscular contraction. No smooth muscle can contract, however, until it has tone, *i. e.*, it must be shortened and resilient, ready for contraction when the stimulus comes. Without tonicity we get no rhythmical movements.



The *nervous system* plays an important part. The normal motor power depends upon the harmonious working of the two sets of nervous systems, vagal and sympathetic. The reflexes governing the motor power come through the stomach, the duodenum and jejunum, as, also, through psychic causes, and all sorts of reflexes may arise from the whole sensory periphery (*e. g.*, appetite, exercise, etc.). Tone for example is absent in general weakness of the body, as well as that of the nervous system, and without tone we get hypomotility. The propulsion of food is governed partly by the amount and character of the gastric secretion. Normally the passage of food is controlled by the duodenal mucous membrane, in other words, only as much food is passed through as can be utilized by the alkaline juices; if no acid exists we may get hypermotility because there is no acid to be utilized, *i. e.*, hypoacidity induces hypermotility, and *vice versa*, hyperacidity and hypersecretion may induce stagnation either from atony or from pyloric spasm, the latter induced by the irritation.

Cannon has shown that the rhythmic movements of the antrum are regulated by the action of HCl and it is the acid which keeps the cardia closed. The secretory values depend so much on motility that our methods of estimating increased HCl seem nowadays rather inaccurate. The normal gastric juice with atony may give hyperacidity to our tests, while if hypertonus exists a diminished HCl may be apparent. It certainly seems in view of the importance of motility in its relation to secretion, that our older classifications of hyperacidity and hypersecretion need some modification.

Certain *mechanical factors* influence motility. (1) The amount of food in the stomach and (2) its consistence. The more food in the stomach, the quicker is this motility due to the distension (within limits), which acts as a stimulus to contraction. The fundus contractions are greater, the peristalsis of the pylorus is more energetic, and the intervals between the contractions are shorter.

All grades of motor insufficiency occur from mere atony to extreme gastrectasis, although whether these may be etiologically linked together is uncertain. Two conditions must exist to establish a rational use of the term gastrectasis—there must be enlargement of the organ and impairment of its motor power. The impairment may be merely relative, that is, the muscular activity may be greater than is normal, as when a pyloric stenosis hinders the rapid outflow. This terminology applies, however, only to the chronic forms, for the acute variety of dilatation is essentially a different condition and to be considered separately.

**Acute Dilatation of the Stomach.**—This is probably more common than is generally supposed, and certainly as a terminal feature in pneumonia and cardiac disease, as well as a complication in surgical conditions, it is by no means rare. German students have been described by Riedel as commonly affected after beer-drinking bouts, and it has followed other errors and indiscretions in the diet. Brinton referred to the condition fifty years ago, although Fagge first gave prominence to its clinical features. He recorded two fatal cases in patients eighteen and thirty years of age, in whom the stomach filled up rapidly with fluid. His

description holds good today as one of the most complete pictures of the condition. Campbell Thompson, in 1902, collected 44 cases, and Neck, in 1906, recorded 60 instances. The most recent reviews of the subject are by Conner,<sup>1</sup> who analyzed 102 cases of the disease (1907), and Laffer, who collected 217 cases in all.

**Etiology.**—Various degrees of dilatation occur involving the stomach alone, the stomach with the duodenum, the stomach with the duodenum and jejunum, or the stomach with even a larger area of small intestine. This indicates that the causes must be varied and the pathogenesis different in various instances. There are predisposing and exciting causes, although it is not easy to dissociate these in all cases, all the more so as the etiology is apparently not only varied but often not to be determined at all.

1. *Debilitating Conditions.*—(a) *General, e. g.,* anemia, rickets, toxic states, certain infections, especially pneumonia, typhoid fever, and miliary tuberculosis, also cardiac disease (Goodhart). These may be the result of various influences which alter the muscular tone of the stomach wall, either indirectly by affecting nervous control, or more directly by toxic action on the muscle. There may be perhaps a neuromyopathy, with spasm of the pylorus and stenosis, although, as Conner and others have suggested, the theory is unstable in view of the constant presence of bile in the vomitus in such cases. Nevertheless, the very sudden onset in many of these patients suggests some special circumstance which the toxic state or nerve lesion has favored. The condition is common in children with rachitic manifestations. In one case of pneumonia under personal observation the dilatation came on without warning, in a patient who had shown no signs of any gastric distress or abdominal distension half an hour before the extreme dilatation and agonizing symptoms had reached their full development. Lavage was at once performed with immediate relief and disappearance of the enormous distension tumor. Six hours later the symptoms recurred quite suddenly with similar results, the patient having rested quietly without signs of distress or distension in the interval. (b) *Local:* Previous gastric disease may predispose to the condition, usually through fermentation, giving rise to what has been termed the “gaseous form” of acute dilatation. This is often combined with the etiological types. Excessive secretion has been regarded by some as the primary cause, although there is little to support the view.

2. *Trauma.*—Various forms of trauma are associated with acute dilatation: Head injuries (Erdmann, 1868, Thomson, etc.), with supposed lesions of motor nerves. Spinal injuries, with or without cord symptoms; in one instance (Edmunds) the dilatation appeared five weeks after a paraplegia. Blows on the abdomen (Wallace and Box).

3. *Postoperative or Postnarcotic.*—These cases, which are numerous, are remarkable in that few have been recorded in which operations on the stomach itself preceded the dilatation. Abdominal operations of various kinds (gall-bladder, uterus, ovary, kidney, appendix, etc.), as

<sup>1</sup> *Amer. Jour. Med. Sc.*, 1907, cxxxiii, 345.

also operations on the extremities for a great variety of conditions have been followed by acute gastric dilatation. The interval between anesthesia and the advent of gastric symptoms varied. In most cases the dilatation followed closely upon recovery from the effects of the operation and anesthetic; in others, days or weeks intervened. James Bell's statistics from the Royal Victoria Hospital are of interest in this connection. There were 12 instances which followed various abdominal operations; some accompanied general peritonitis; in a few, definite gastromesenteric ileus was present, while in others no cause whatever was found. Several of the milder cases recovered completely.

The evidence tends to show that in many instances there is a paretic condition of the gastric muscle, associated with some toxic condition of unknown origin. Bloodgood has given an analysis of cases observed by him after operation and in association with varying causes, one of the principal being the obstruction which occurs at the junction of the duodenum and jejunum (gastromesenteric ileus). In these cases the enormous distension of the stomach and duodenum is characteristic, and is to be differentiated from high occlusion of the small intestine. Doubtless with acute dilatation there may be additional dilatation of the duodenum with or without constriction at the mesentery, and in other cases, again, much of the small intestine may be concomitantly dilated. The diagnosis of the exact site of the obstruction (if this exist) has an important bearing on the selection of the treatment.

4. *Traction on the duodenum* or pressure upon it from various conditions, especially a low situation of the small intestines in the pelvis, is no doubt a common cause. Here the tightened mesentery may incarcerate the duodenum as it lies on the vertebral column and produce the condition (Kundrat). Albrecht, however, regarded this as a result, and not as the cause of the dilatation. He believed that through dilatation of the stomach the small intestine was held low in the pelvis, and thus pulled upon the mesentery and indirectly compressed the duodenum. This "arteriomesenteric incarceration" thus aggravated the already existing gastrectasis. Whatever be the cause, certainly a large number of cases show at autopsy this constriction of the duodenum, and Bäumler's beautiful anatomical proof is especially worthy of mention. In his classical case there was a very localized constriction near the lower end of the duodenum where it was crossed by the mesentery, and in the mucosa there was a well-defined circular necrosis corresponding to the external compression.

Albrecht had already demonstrated the fact that at this point the duodenum, even under normal conditions, is more flattened than round, because of the pressure of the overlying mesentery with its superior mesenteric artery, and, as Conner points out, this may be readily demonstrated in the cadaver, as also the increase in the constriction, by gentle downward traction on the mesentery with the finger inserted in the duodenum at this point. The three things considered essential to this are "the dorsal decubitus, an intestine nearly or quite empty of gas and feces, and a mesentery of suitable length—long enough to permit the intestines to slip into the pelvis and yet not so long that they may be



supported by the pelvic floor." Perhaps it may be for this reason that lobar pneumonia is sometimes complicated by acute dilatation, owing to the weight of the lungs and violent coughing (Lehmann).

5. *Deformities of the spine* have been frequently observed in patients developing acute dilatation, and in many cases the orthopedic surgeons have been the first to observe the condition. Doubtless in these cases dietetic errors leading to fermentation and distension were often the exciting cause, while the restricted cavity of the trunk accounted in part for the onset of symptoms. In other cases perhaps the vagus has been indirectly acted upon and the control of peristalsis interfered with.

6. *Pressure of a kidney* which had been surgically fixed was the cause in one instance (Oppenheim).

7. *Dietetic Errors*.—Possibly too much or unsuitable food may directly induce acute dilatation by fermentative processes and distension; such are the repeatedly quoted cases in which one meal or one indiscretion preceded the symptoms. Sometimes the combination of great fatigue followed by dietetic indiscretions has seemed to be the direct cause, and sometimes the compression of a plaster jacket, together with errors in feeding, may have accounted for the onset.

8. *Spasm of the cardia and pylorus combined* was believed by Kelling to initiate the symptoms, although the frequent absence of these conditions scarcely bears out this view. Perhaps the association of hypersecretion with acute dilatation, to which special attention has been drawn by Heile, belongs to this category.

9. *The pancreas* is thought by some to have some relation to acute dilatation, and Bardenheuer mentions one instance following traumatic pancreatitis which was cured by gastro-enterostomy. Hoffmann, too, describes a case in which chronic pancreatitis and multiple necroses were intimately associated with acute dilatation.

**Pathology.**—The stomach is usually of enormous size, often extending down into the pelvis, and may be bent in an irregular U-shape, with the largest half at the fundus. The color is bluish, purple red, or pale; the wall is often thin. Definite pyloric obstruction is rare. The duodenum is dilated partially or throughout in half the cases. Sometimes the dilatation definitely stops near the lower end of the duodenum where the mesentery crosses, and may compress it against the vertebral column. At other times the dilatation extends throughout the whole of the small intestines.

**Symptoms.**—Mild and severe cases are found, the mild ones being slow of cure, with emaciation, weakness, and prolonged convalescence. The symptoms are usually acute and without previous signs of gastric disease, closely resembling those of intestinal obstruction, for which, indeed, they are frequently mistaken. There is acute abdominal distress with distension of the area to the right of the midline and beyond it. There is pain in the epigastric or umbilical region, or perhaps in the left hypochondrium, with dyspnœa, increase in the pulse and respiration rates, but no fever. Vomiting, which is almost invariably present, appears early, as a rule, and is persistent. The vomitus is a dark brown fluid, very abundant, often amounting to many quarts, containing bile

and sometimes traces of blood. The odor is usually foul but not fecal. Analysis shows that HCl is a very variable quantity and that lactic acid is sometimes present. Hydrogen sulphide has been noted in several instances. Lavage, if carried out, empties the stomach of liters of such contents, the removal of which gives immediate relief. Constipation is the rule; the urine is diminished and of high specific gravity, because concentrated, and there is marked thirst which is not easily satisfied.

**Objective Signs.**—*Inspection* often shows the outlines of a distended stomach, which disappear partially after vomiting, and totally after lavage. There is no visible peristalsis in the majority of cases. *Palpation* shows tenderness and sometimes the firm, tense cushion of the dilated stomach, and but little else, unless increased resistance in the left hypochondrium. Sometimes tenderness is absent, although this is not usually the case. A succussion splash is almost invariably obtained. *Percussion* shows diminution of the tympanitic gastric area and its replacement by dullness, especially in the left side of the abdomen and below the navel, reaching up as high as the right costal margin. This is an important diagnostic sign. In fatal cases there is collapse with the hippocratic facies; in case of recovery the stomach returns to its normal size in a few days or weeks.

**Diagnosis.**—The condition is usually mistaken for some acute abdominal disease, especially perforative peritonitis or intestinal obstruction, and operation is frequently undertaken unnecessarily. The diagnosis requires a careful anamnesis. Of 60 recorded cases, only 13 were rightly diagnosed. The diagnostic features are the onset, with pain, collapse, and absence of fever, abdominal distension and localized left-sided dullness, with uncontrollable vomiting of large quantities of fluid containing bile, and having no fecal odor. The relief of symptoms and signs after lavage and postural treatment (knee and elbow position) are important confirmatory signs. The differential features of high intestinal occlusion are mentioned by Bloodgood as follows: "Initial pain, accompanied perhaps by peritoneal shock, which may later somewhat disappear, and vomiting without marked distension." In acute dilatation the initial pain is often absent, there is epigastric distress and gradual and progressive collapse. Epigastric distress is early and relieved by lavage in acute dilatation, but is much later in high intestinal obstruction.

**Prognosis.**—The outlook is bad if the diagnosis be not made early and suitable treatment adopted; 47 out of 64 cases published died. In Conner's series of 102 cases, 74 died, although, as he remarks, many unreported cases recover where either the condition was mild or unrecognized. In 75 per cent. of Conner's cases the duration was less than five days, and in a few instances the patients died within three hours from the onset of the symptoms. If the complication does not end fatally, some impairment of motor power usually persists. The symptoms may disappear at once after treatment, or days and weeks may elapse before complete recovery.

**Treatment.**—Early lavage is essential, with the head low and the pelvis high; one is otherwise very apt not to reach the fluid at all. It

is of great importance to thoroughly wash out the organ, at first often, later on less frequently. No food should be given by the mouth until recovery has sufficiently advanced, and one should use water enemata or subcutaneous saline infusions instead. Stimulants should be given as required. Operation is of no benefit unless after lavage there is no improvement, in which case some severe intestinal obstruction may be suspected. In these cases the probable incarceration of the duodenum requires special treatment. Schnitzler first pointed out the benefits to be gained by turning the patients over from the dorsal position, and Bäumlér recommended the knee and elbow posture as having been successful in two of his cases.

When such measures fail, operation may be tried, although hitherto the results of gastro-enterostomy have been far from encouraging. Bloodgood's study of the condition has led him to believe that it is well to regard these cases as probably instances of gastroduodenal dilatation, and if lavage fails the duodenum should be carefully explored. If the dilatation be purely gastric, then gastrostomy or gastrojejunostomy should be performed, whereas if the duodenum too is involved, jejunostomy or duodenojejunostomy is preferable. Borchardt, quoted by Conner, states that when other methods of treatment have failed, it is doubtful if operation will meet with any greater success.

**Chronic Dilatation.—Varieties.**—There are two forms: (1) Idiopathic, or absolute, otherwise called primary or atonic; simple gastrectasis; myasthenia gastrica; and (2) symptomatic, or relative, otherwise called secondary or obstructive—the result of stenosis of the pylorus—usually hypertonic and mechanical. There is either benign or malignant obstruction and rarely the duodenum is the seat of the stenosis. Allbutt suggests the term extension as including especially the cases of idiopathic dilatation. A differentiation of the main forms is not always possible, either clinically or at autopsy, for cases with pyloric spasm, which has been the supposed cause of the atony, will often show no visible lesion. The idiopathic form is milder and rarely with retention; the secondary nearly always shows retention. The very existence of a true idiopathic condition is still a matter of doubt to some.

The diagnosis of *idiopathic dilatation* can only be made by prolonged observation to exclude stenosis. The proof of its existence lies mainly with clinical medical experience and surgical findings at operation. It has certainly fallen to the lot of every medical man of any experience to successfully treat individuals with a marked idiopathic gastrectasis. Gastric analysis shows retention of food, with all the evidence of gastrectasis, and the absence of further developments should suffice to prove the existence of a dilatation due to causes other than stenosis. Surgeons, too, find such a condition not uncommon, and operate for gastrectasis when careful search fails to reveal any signs of obstruction at the pylorus. Mikulicz evidently thought them not infrequent.

**Idiopathic Dilatation.**—The walls lose their resiliency and the viscus expands, becoming gradually more unable to handle the ingested food, especially when in large quantities. From various causes atony and temporary distension are produced. If the cause acts often enough,



long enough, and severely enough, the elasticity diminishes, the tonus is wanting, and food is retained, and dilatation is the result.

**Etiology.**—It occurs most commonly in adults of middle age, although it is not infrequent among rachitic children (Ladd). Two classes of causes exist, local and general. It may be taken for granted that in many cases, simple atony, the result of manifold local and general conditions, is one of the most common predisposing antecedents of idiopathic dilatation. *Local conditions* are trauma, improper clothing, laparotomy, repeated pregnancies, chronic gastric disease of any kind, especially if with fermentation (Cohnheim's so-called vinegar and gas factory) and excessive improper food, whether in quantity or quality.

Kaufmann describes two classes of patients: (1) In the one there is variable secretion (high or low), with atony; the symptoms are really due to the atony, and are cured by lessening it. (2) In the second there is variable secretion without atony. Such cases come under the category of neuroses, *e. g.*, hyperesthesia of the gastric mucous membrane, and resemble similar conditions in other organs (*e. g.*, cardiac neuroses, nervous diarrhoea without excessive mucus, dyspnoea without lung trouble, etc.); *i. e.*, gastric neuroses so-called. Such patients need no local therapy for the stomach but rather general treatment. In such cases the secretions remain abnormally high or low, and yet the symptoms disappear because depending on a general neurosis, which when cured is accompanied by an alleviation of the local symptoms. Certainly in gastrectasis the HCl secretory changes alone are mere accidents in the symptomatology and must not be given too prominent a place. Usually when the motor power is repaired any symptoms supposedly due to hypersecretion or hyposecretion will disappear.

Gastroptosis frequently accompanies gastrectasis. It is quite conceivable and it very often happens that when gastroptosis exists in excessive eaters the persistent overloading of the stomach will cause more and more descent of the organ, with the result of finally causing a kink at the duodenum—as may occur in the cases which show the crescentic horizontal variety of gastroptosis. A progressive stenosis with increasing motor insufficiency may occur. Steele and Francine found on examination of 70 patients with gastroptosis that dilatation existed in all. The degree, however, must be very slight when one considers how extremely common it is to find gastroptosis when absolutely no signs or symptoms of indigestion exist. This fact alone should indicate that except under certain other predisposing conditions, gastroptosis does not generally cause gastrectasis, even though it frequently precedes and more often follows it.

**General Causes.**—A *hereditary weak stomach* is recognized as a factor of some importance, and predisposition to chronic dyspepsia certainly exists as a family weakness. *Chronic constipation* is regarded by Ewald as a source of gastrectasis. The persistent inactivity of the intestines or their paresis leads to diminished gastric peristalsis and atony. So also may any intestinal disease. General causes assist the local conditions and thus aid directly and indirectly in inducing dilatation, for local causes act more forcibly in stomachs rendered susceptible through

*prolonged illness* or general *myasthenia*, be it *organic* or *neurotic*. The cause may be toxic or muscular, *e. g.*, in *sepsis*, *typhoid fever*, *tuberculosis*, and *pernicious anemia* (whether it be that toxins weaken the wall or the muscle be altered through the anemia and malnutrition. The same holds in *chlorosis* and in repeated hemorrhages). *Toxic causes* act either generally, *e. g.*, *tobacco*, or both generally and locally, as in the case of alcohol. A *busy life* with no rest after meals and hasty eating is often an antecedent cause. Thus it is with musicians of sedentary habits, neurotics, and hypochondriacs. Venereal excesses are regarded by some as a factor in the etiology. Anything which induces *general weakness* may be regarded as a predisposing general cause.

**Relative, Symptomatic, or Obstructive Gastrectasis (From Stenosis).—**The causes of stenosis are numerous; spasm with gastric ulcer, erosions and scars (never from neuroses) (Cohnheim); foreign bodies: *e. g.*, resin balls from swallowing shellac spirit for ten years, hair balls, cherry stones (Crämer), gallstones and beans and peas (Fleiner), (such bodies may remain for three months); hypertrophic pyloric stenosis; polypi; tumors (Crämer); scarred ulcers; cancer of the pylorus and of the lesser curvature extending to the pylorus. Tumors outside the stomach (*e. g.*, of the liver or gall-bladder, pancreatic tumors pressing on the duodenum, floating spleen with pressure on the duodenum, movable kidney, dermoids, enlarged glands, etc.) may be a cause. Perigastritis: inflammation outside of the stomach and associated with neighboring organs, *e. g.*, liver, gall-bladder, pancreas; cicatricial puckering associated with cholelithiasis, perigastritis, etc.; epigastric hernia; appendicitis with or without adhesions; omental adhesions from appendicitis, especially if to the linea alba; torsion, flexure, and kinking of the duodenum at the duodenojejunal fold in enteroptosis; trauma, producing inflammations near the pylorus, hematoma of the wall, or spasm of the pylorus.

**Pathology.**—The dilatation varies in degree and character. The one anatomical feature is the altered size of the organ, although that is not always increased even with marked motor insufficiency; sometimes it is monstrous and may seem to fill the entire abdominal cavity. In Strauss' case of stenosis from an old ulcer the stomach held five and a half liters. Much larger dilatations are mentioned. Jadow's case in which the capacity was 45 liters is worthy of mention, if true.

The gastrectasis may be partial and is sometimes diverticular. Dilatation begins in the lowest portions and those most overtasked, the fundus, pylorus, and greater curvature. Later it becomes general. The other abdominal viscera are in extreme cases compressed and pushed in various directions. The spleen and liver may lie abnormally high while the small intestines are pushed downward. The thickness of the stomach wall varies. In one case with chronic inflammation (Lebert) it was 14 mm. thick. It is especially in the obstructive cases that this increase occurs, although even in idiopathic cases it may be abnormally thick. As a rule, when no stenosis exists the gastric wall is thin and atrophic. The mucous membrane may be thickened, hypertrophic, or irregular and hard, a condition usually existing when chronic gastritis is also present. Sometimes the mucosa is thinned and atrophic, and not

at all infrequently atrophy and hypertrophy alternate in the same mucous membrane. The muscle is changed, its appearance depending on the cause and pathological condition. With pyloric stenosis, especially if benign, there is muscular hypertrophy (compensatory), while in idiopathic cases the atrophied muscle is but a feature of the general myasthenia. Fatty and colloid changes are often seen in microscopic preparations. The interstitial tissue is often infiltrated in the chronic cases with increased fibrous tissue and small round cells, while in the acute cases there may be small round cells, extravasated blood cells, and separation of muscle and fibrous tissue cells.

**Symptoms.**—These vary according to the degree. In mild cases there may be but a few digestive disturbances, mental torpor, thirst, anorexia, constipation, and diminished urine, with little evidence of any serious condition. This, too, occurs in the early stages of the more serious types. Advanced cases from whatever cause show certain general symptoms in common. The general appearance of the patient shows emaciation, but a fair color is preserved. The skin is naturally dry because of retention of fluids in the stomach, and the extremities are often cold.

*Dyspeptic symptoms* develop early. The appetite is usually diminished (unless hyperacidity exists from some benign stenosis), the breath is sour, and flatulence and pyrosis are present. Thirst is an important and often a distressing symptom. Water not being normally absorbed in the stomach, the degree of thirst corresponds to the amount of retention and the degree of motor insufficiency, of which it is therefore a good criterion. *Constipation* is marked, because no water is passed into the intestines, and there is atony of the bowel. Dry, hard scybala are often passed with colicky pains; piles and fissures form. The degree of constipation is also a good criterion as to the degree of motor insufficiency. *Diarrhœa* is rare, and sometimes alternates with constipation; mucous colitis may co-exist. *Emaciation* occurs in proportion to the degree of dilatation, and is worse if the intestines are deranged.

*Pain* is less marked in idiopathic than in obstructive cases. In obstructive cases, especially if from ulcer or spasm, or cancer, it is often intense. Sometimes, even in cancerous dilatation, there is no pain. *Vomiting* is not so constant in idiopathic as in obstructive cases. In the latter it is the rule because the food cannot pass, and the stomach empties itself by emesis. A feature of the vomiting is its periodical occurrence and explosive type after every few meals. The amount has no relation to the previous meal, and the vomitus consists of food from days or weeks before. It is thus copious, and may amount to several quarts. Later there may be little or no vomiting because the walls are weakened, a condition which is of course serious. The general appearance of the individual foodstuffs depends on the character of the gastric secretions. The color is usually of a dark gray brown. There are three layers, froth on top, fluid in the middle, while the sediment below contains yeast, sarcinæ, mucus, and food (new and old). Mucus, if abundant, indicates a probable gastritis. Microscopically, one sees bacteria, fatty acid crystals, epithelial cells, sometimes blood cells and pigment. There is an odor of fermentation and organic acids may be abundant. The finding



of lactic acid is important only when in the fasting contents or after a test meal; moreover, Strauss maintains that lactic acid from ferment action does not appear in the stomach if 0.12 per cent. HCl (total) is present. Vomiting gives temporary relief even although it only partly empties the stomach. HCl may be in excess, deficient, or normal.

*The Urine.*—Corresponding to the amount of retention, so is the diminution in the renal secretion. It forms a good basis for measurement of the gastrectasis and is also a guide to prognosis and treatment. Small amounts indicate a more serious form, and suggest the use of water enemata at regular intervals. Increase in the urine indicates improvement. The urine when diminished is concentrated and has a high specific gravity. The chlorides are lessened and the phosphates increased. If much hyperacidity is present the urine may be alkaline. Albumin and also acetone and diacetic acid are sometimes present.

*Cardiovascular symptoms* are common: Palpitation, anginoid attacks, dyspnoea, and throbbing sensations. The pulse is often weak and irregular and the blood shows secondary anemia. Old heart lesions and many chronic febrile conditions exhibit gastrectasis in their terminal stages.

The *temperature* is lowered and the patients feel chilly from slight causes. More rarely there are febrile attacks from a concomitant gastritis or toxic causes.

*The nervous symptoms* are varied. Languor, apathy, depression of spirits, and melancholia are common features. Headache and dizziness are frequent. Mild psychoses, insomnia, deafness, etc., are common manifestations, and when coming on at a regular time are regarded by patients as the cause rather than the effect of the malady. These are probably the result of dryness of the tissues, inanition, and toxemia.

*Tetany* is worthy of special notice. Mentioned by Morgagni, it was first described by Newman in 1861, and later by Steinheim, while Kussmaul gave it prominence as a classical feature of dilatation in his description of gastrectasis and its treatment by the stomach pump in 1869. This condition, although common to various diseases of the gastrointestinal tract, is chiefly associated with pyloric obstruction in which dilatation, hypertrophy of the stomach wall, with hyperacidity and hypersecretion are present. It is thus more commonly associated with benign stenosis, and is rare in obstruction from malignant disease or from external pressure. It is probably induced by the absorption of some poison which is not neutralized in the stomach. The attacks appear after severe and persistent vomiting, and after lavage, and are associated less with the act of vomiting than with the presence of putrid contents in an overfilled stomach. The stomach should be emptied some hours before lavage is practised to avoid the onset and recurrence of the attacks. The duration may be from a few minutes, to hours, days, or weeks. When prolonged it ends usually fatally. Mild grades are common and probably often overlooked. Muscular twitchings, prickling sensations, etc., in gastrectasis are doubtless warnings to urge surgical intervention. Crämer's view was that any gastrectasis not vastly improved in four weeks under lavage, dieting, and massage should be subjected to operation.

Various theories exist as to the causation of tetany. Kussmaul

regarded it as due to dehydration of the tissues—nerves and muscles—on the analogy of the occurrence of cramps in Asiatic cholera, an analogy which, however, is scarcely justifiable, inasmuch as the same cramps occur in the so-called cholera sicca in which dehydration of tissues takes no part. Later on Kussmaul himself disclaimed the theory, although Fleiner, Albu, and others still maintained it. Germain Sée held the theory of its causation by reflex action from stimulation of the sensory nerves of the stomach, *e. g.*, after lavage, vomiting, etc., and its frequency in sucklings, its occurrence with intestinal parasites and disappearance after their removal, suggest this possibility. Gerhardt regarded the complication as the result of a poison, basing his views on the nervous symptoms, some of which resembled those of alkaloidal poisonings. Bouveret and Devic originated the theory of auto-intoxication from the prolonged action of abnormal processes of digestion, and this theory holds its preëminence up to the present. In proof thereof they isolated a substance soluble in alcohol, resembling Brieger's peptotoxin, which when injected into animals caused general convulsions. Opponents of these experiments held that the convulsions were not of the nature of tetany, that alcohol alone could induce similar attacks, and that untreated gastric contents are incapable of inducing such symptoms. Dickson tried the injection of gastric contents in various ways to produce tetany but without success.

Indican has often been found in the urine of patients suffering from gastrectasis with tetany. Acetone has been found in the stomach, but not in enough quantity to do harm, because oxidized.

*The prognosis* in tetany is always grave, and the average mortality has been given as 70 to 80 per cent. There were 31 deaths in 40 cases (Albu). Death usually follows only after the tetany has been well developed, from failure in treatment. Patients who pass successfully some attacks of tetany, are liable to recurrence of attacks.

*Treatment of Tetany.*—Medical treatment may be tried for a short time, but surgical interference should not be delayed too long when lavage and medicines fail. Careful washing of the stomach should be beneficial. Greenfield suggested after careful lavage with some mild antiseptic a final washing with a solution of sodium phosphate and then the introduction of about ten ounces of boiled milk containing sodium phosphate in the proportion of one dram to a half-pint, diluted with hot water. The one efficacious method is the surgical one which provides proper drainage by performance of a gastro-enterostomy.

**Physical Signs of Gastrectasis.**—These vary greatly, especially according to the cause and extent of the condition, for cases of primary or spastic dilatation show no tumor.

*Inspection.*—This is very important. The prominence of the stomach may be visible, although in mild cases there is usually nothing abnormal seen. The stomach is seen better if stenosis exists, because it is then less flabby and more hypertonic. The abdomen is usually flabby, the stomach much enlarged, and the outline of the greater curvature may perhaps be visible down as far as the pubis. Unless ptosis is also present the lesser curvature remains high in the epigastrium. Inflation may aid

in locating the organ. *Visible peristalsis* is rare without obstruction. With pyloric stenosis it is either spontaneous or induced by flicking the abdomen with a wet towel or the finger. A tumor-like prominence appears in the left hypochondrium, which swells, falls, and re-appears to the right. Antiperistalsis sometimes exists.

*Palpation* should be done systematically, carefully and gently with the flat hand first, then following the respirations, examining with the patients in various positions, and even in doubtful cases with the aid of an anesthetic. In idiopathic dilatation one gets merely a sense of the air cushion present, and this more definitely tense with obstruction, while sometimes one can feel gas passing the pylorus. Boas lays stress on the importance of palpating for contraction of the stomach, both stiffening and rigidity (so-called *Magensteifung*) and peristalsis. The *percussion splash* has a certain value. The presence of a succussion splash is only of value if used when the stomach would be empty under normal conditions, *i. e.*, seven hours after a meal. The splashing which neurasthenics can voluntarily induce by contraction of the abdominal muscles is of course not to be confused with the above, for it may be performed without gastrectasis and even when very little fluid is present.

*Percussion* determines the size of the organ, or at all events its outlines. There is a deep tympany over the stomach, the extent depending upon its size and situation. Dehio's percussion tests after drinking water may be mentioned. Dulness may be found below when the patient is in the upright posture, if much fluid is present. Sometimes the dulness is more to the left, and changes with position and after emptying the stomach. This is merely a slight aid to diagnosis and only to be used with insufflation tests as well. Absence of liver dulness may exist and depends on the position of the hepatic flexure and is not in itself a reliable sign of any pathological state. Percussion affords us no information as to function. *Auscultatory percussion* has not as yet given the satisfaction hoped for; Broadbent recommends it, Allbutt does not. Certainly control tests do not prove it infallible for outlining the borders of hollow viscera. Too much depends on the nearness of the scratching or percussing finger and on many other factors which alter the note.

Examination with the  $x$ -rays after the administration of bismuth subnitrate may enable one to see the outlines and the less active fundus; one may also see the pylorus open intermittently and the impaction of masses in imperfect solution prolonging the closure of the pylorus.

The salol and potassium iodide tests are unreliable. The desmoid test is also of doubtful value, depending much on the quality of the material used.

*Stomach Contents.*—The essential feature is the abnormally large quantity of food returned after a test meal. This alone is a proof of motor insufficiency and is pathognomonic. Chemical examinations give varying results according to the primary cause of the dilatation. In the milder forms, depending on idiopathic conditions, HCl is usually diminished or normal, and rarely increased. In the obstructive forms it is excessive or normal, rarely diminished unless late on, and then chiefly in cancerous and atrophic conditions. Bile may or may not be present.



Varying evidences of fermentation exist (lactic acid, yeast, gas, etc.), according to the conditions present. Thus, while lactic acid is commonest in malignant disease, gaseous fermentation with hydrogen sulphide is usually an indication of benign stenosis. The production of gases is not prevented by the presence of HCl, nor is albuminous putrefaction; in fact, the latter is usually only present when HCl is there. The motor insufficiency, not the secretions, is the *cause* of the gas fermentation. The state of the secretions determines the degree of digestion of foodstuffs after test meals. Microscopically the findings differ according to the cause of the dilatation, *i. e.*, whether benign, malignant, etc.

*Benign pyloric stenosis* gives special features to the clinical picture of gastrectasis. The earliest physical signs arouse suspicion when the past history yields some cause for a stenosis. Distress appears soon after dietetic errors and the symptoms increase slowly but progressively. The two predominant subjective features are pain and vomiting. The two predominant physical signs are visible peristalsis and evidence of a tumor. Gastric analysis usually shows increased hydrochloric acid secretion, and microscopically there are yeast cells and sarcinae.

The *pain* soon follows upon the early feelings of mere distress. It comes on chiefly after food, and while periodic or intermittent, it recurs with ever increasing frequency and often with progressive intensity from week to week, and sometimes is almost continuous. Later, as retention of food occurs, the pain may be nocturnal, associated perhaps with hyperacid secretion, fermentation, or dependent on the special nature of the obstruction at or about the pylorus. Often the pain is definitely associated with the increased peristalsis, and is therefore sometimes of a cramp-like nature, especially if hypertrophy of the gastric muscle has occurred. The vomitus, which in the course of the malady follows closely upon the onset of the pain, may consist chiefly of solids. Vomiting occurs often with increasing frequency up to the time when hypertonus gives way to atony, and then the emesis recurs at longer intervals and is less explosive in character.

*Physical Signs.*—The early stages may reveal nothing but a prominent epigastrium or a slight fullness, but visible peristalsis soon appears and should be carefully looked for. Often much patient watching is required before the peristalsis appears. Inspection, further, often reveals the pyloric tumor, sometimes as movable, shifting with respiration or by alterations in the position of the internal viscera. Palpation reveals increased resistance over the pyloric area, and a cushion-like sensation over the viscus itself. In thin, flabby persons the tumor may be palpable quite early. Movability is a characteristic feature of non-adherent pyloric tumors resulting from scarred ulcers. They may often be shifted to widely different areas of the abdomen, are usually not very sensitive, and do not seem to be very nodular. Bouveret described a sign which he calls intermittent gastric tension. In the recumbent posture the left side of the epigastrium is more prominent than the right, and on gentle palpation is balloon-like to the feel; during palpation, however, the swelling disappears, re-appearing very soon, off and on, and especially after the ingestion of food.

**Diagnosis.**—The various considerations may be tabulated thus: (1) As to the presence of gastrectasis. (2) If present, as to its nature, *i. e.*, idiopathic or obstructive. (3) If obstructive, as to the nature, *i. e.*, benign or malignant stenosis. (4) If probably benign, as to its special form, *viz.*, spasm, foreign body, hypertrophic stenosis, intragastric tumor, extragastric tumor, inflammation, etc.

Gastrectasis must be distinguished from several conditions. *From dilated colon:* One must make repeated examinations at various hours and empty the stomach by siphonage. It is often hard to tell without such tests, and it may be well to inflate the colon from the rectum. The history and symptoms will assist in the decision. Absence of splenic dullness in itself is of little importance in the diagnosis, being merely an aid. One must exclude emphysema, pneumothorax, and diaphragmatic hernia. Moreover, one must look for a cause, movable or diseased kidney, umbilical hernia, tumor, etc. If necessary, an anesthetic should be used. *From Gastropptosis:* In simple dilatation, the lesser curvature is in its normal position, while if there be gastropptosis, the site will be lower than normal, and the position of the stomach may be vertical, horizontal, or otherwise. In simple gastropptosis there is no sign of motor insufficiency after a test meal. The fluoroscope and skiagraphic picture aid the diagnosis. *From Nervous Dyspepsia (without Motor Insufficiency):* The symptoms are out of all proportion to the organic changes, and there are various stigmata of a neurosis. *From Chronic Gastritis:* The stomach is of normal size and the motor power normal or nearly so (unless dilatation co-exists, as it usually does later on). There is a history of the cause, and much mucus is vomited. *From Hypersecretion:* After complete lavage of the stomach on the previous evening there is abundant gastric juice found in the early morning (more than 40 cc. should be present to make a diagnosis of hypersecretion). *From Gastric Crises:* These present one feature resembling gastrectasis, *viz.*, the marked and copious vomiting, not, however, of retained food, but of concentrated gastric juice and mucus. Gastric digestion is usually normal in the intervals between the attacks. Other conditions, *e. g.*, ovarian tumors, dilated gall-bladder, sacculated peritoneal exudates, and pancreatic cysts should offer no difficulty. Sometimes a *spindle-shaped dilatation of the œsophagus* may occasion doubt because of the periodical vomiting of food from previous days. This may be hard to differentiate. The stomach, however, is not enlarged, the introduced tube causes immediate vomiting of alkaline material, while if the tube be pushed farther it reaches the stomach and withdraws acid contents.

*The Differentiation Between Idiopathic (Atonic) Gastrectasis and Obstructive (Hypertonic) Gastrectasis (from Pyloric Stenosis):* Advanced cases are usually readily diagnosed but in early stages, and even in some that are of long standing, the diagnosis may be impossible for a long time. As a rule, one must take the whole history, symptom-complex, and signs into consideration. The following table indicates in a general way the essential features:

	Idiopathic dilatation.	Dilatation from pyloric stenosis.
History.	None, except of dietetic excesses.	Previous ulcer, hemorrhage, gallstones, carcinoma, etc.
Course.	Slow.	Rapid.
Emaciation.	Slow.	Rapid.
Pain.	Little or none.	Marked.
Vomiting.	Infrequent and copious, liquid and incomplete. Less painful.	Frequent, copious, thick, and mixed with much solids, and complete. Accompanied by pain.
Dilatation.	Moderate as a rule.	Extreme.
Visible peristalsis.	Absent.	Present, and often very marked or easily induced.
Tumor.	Absent.	Often present.
Lavage.	Quick inflow, slower egress.	Perhaps slow ingress, but rapid exit. Expression is easier and often explosive.
Therapeutic tests.	Improvement marked with lavage, etc.	No improvement, but progressive decline in spite of lavage.

**Varieties of Pyloric Stenosis.**—*Pylorospasm*.—This occurs at the height of digestion, as a rule, and may be constant or periodical, resulting in temporary closure of the pylorus with retention of food. There may be severe pains, vomiting, and signs of motor insufficiency, such as thirst, diminished urine, constipation, and enlarged gastric area. The vomitus is hyperacid, and there is often hypersecretion. The vomiting relieves the discomfort until the cycle recurs. Analysis shows stasis, increase of HCl, sarcinae, yeast, fatty acid crystals, and signs of marked fermentation. The pyloric area is tender and may show tonic contractions, while palpation of the fundus may reveal the characteristic rigidity (*Magensteifung*). The prognosis is more favorable, although recurrences are frequent.

*Cicatricial stenosis of the pylorus* (the type is the scarred ulcer, although caustics, etc., may induce it). The history is of importance, especially the record of previous hematemesis or of recurrent attacks of vomiting and pain ("indigestion"). The signs of progressive stenosis, as seen on physical examination, gastric analysis, and examination of the stools for occult bleedings, are likewise important.

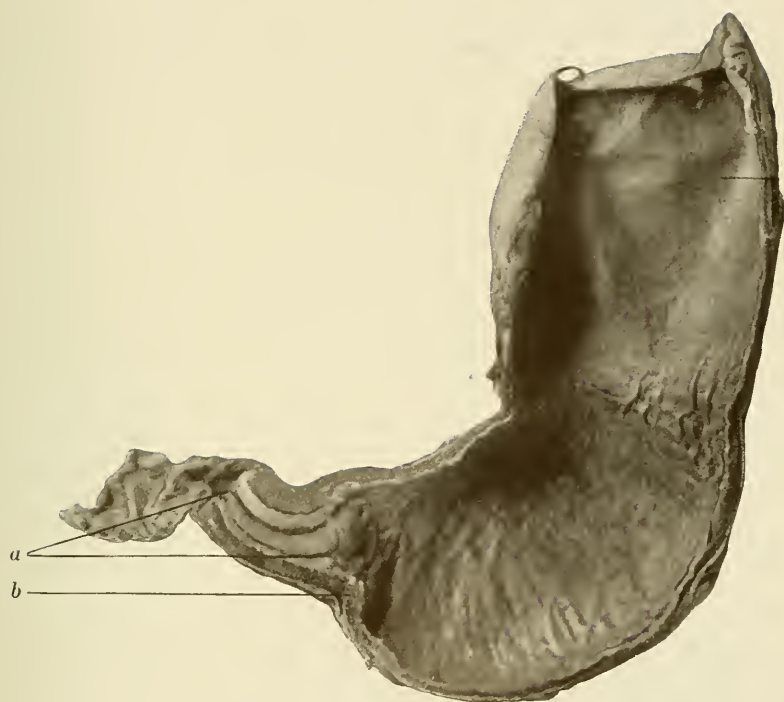
*Duodenal stenosis* may be indistinguishable, unless the obstruction be infra-ampullary, in which case there will be a constant back flow of bile into the stomach. Stenosis of the duodenum usually occurs from cancer, pressure of benign tumors, scarred ulcer, localized peritonitis, gall-stones, malformations, etc.

*Perigastric adhesions with pyloric stenosis* (cholelithiasis, inflammation, etc.). Here, too, the history is of great importance, also the physical signs, the presence of jaundice previously, and the existence of traces of bile in the urine.

*Stenosis from external pressure* occurs from enlarged glands, dermoids, new-growths, and inflammatory exudates, also from kinking or constriction through fibrous bands, etc., as also from traction as occurs in acute dilatation where the duodenum is constricted through traction of an arteriomesenteric fold.



PLATE X



Congenital Stenosis of the Pylorus.

*a*, pylorus; *b*, hypertrophied muscularis.



*Impaction of food or foreign bodies* in the pylorus may be the cause of *benign tumors* within the pylorus, *e. g.*, polypi.

*Hypertrophic stenosis*, the so-called stenosing gastritis. The condition is probably a rare one, arising from different causes and presenting as its two main features at first a chronic gastritis and later the signs of motor insufficiency with stenosis. There are no cicatrices and no tumors, but a diffuse thickening of muscle or fibrous tissue may be present, a localized benign stenosis. Quite a number of isolated cases are on record (Boas, Habershon, Tassia, Tilger, etc.). The condition has been found most commonly in middle age, runs a slow course over years, with exacerbations and remission of symptoms (chiefly those of gastritis followed by stenosis). There is anorexia and emaciation. The gastric analyses vary. It is not easy to distinguish from a scarred ulcer which may have been latent for years, but the diagnostic features are those found in the general picture with its protracted duration. In recent descriptions by Russell and by Maylard, cases of adult stenosis of congenital origin are described with symptoms of varying intensity, and these writers conclude, whether or not on sufficient proof, that such cases are very common indeed. It seems, however, not always easy to prove the existence of a stenosis during operation, and the mere improvement after gastro-enterostomy should not of itself convince one that a pyloric stenosis had been present—still less that it was congenital.

*Stenosis from Malignant Disease of the Stomach.*—The following table will outline the essential differences from benign conditions causing stenosis:

	Benign.	Malignant.
History.	Ulcer, toxic gastritis, causes, etc.	Previous normal digestion, perhaps.
Age.	Any age.	Usually after forty years of age; not infrequently earlier, however.
Course.	Rapid, but with less marked decline in health.	Rapid and progressive development of weakness, etc.
Tumor.	Smooth, often more movable.	Nodular, hard, fixed.
Secretions and contents.	HCl normal or excessive; no lactic or butyric acid; H <sub>2</sub> S present sometimes; few or no Boas-Oppler bacilli; sarcinæ long present.	HCl less or absent; lactic and butyric acids often present; H <sub>2</sub> S uncommon; Boas-Oppler bacilli common; sarcinæ uncommon, and soon disappear.
Therapeutic	Sometimes nutrient enemata benefit.	Nutrient enemata useless.
Metastases.	None.	Usually sooner or later.

**Course of Gastrectasis.**—The cause determines not only the duration but also the essential features and symptoms. Idiopathic cases are slow in development, and their course depends on the persistence of the exciting cause and the possibility of its removal. Patients who have long been the victims of the disease in an advanced stage will be difficult to relieve. With early and suitable treatment the condition is often held in check and development will extend over years. Thus the idiopathic cases and those due to pylorospasm, being more amenable to therapy, will run a mild course and last a shorter time than those associated



with stenosis. Pyloric obstruction causes a more or less rapid development of symptoms, rapid where the obstruction develops quickly, as in carcinoma, subacute perigastritis, etc., more slowly with gradual cicatrization of an ulcer at the pylorus. Where benign stenosis exists, its special nature, its degree, extent, and curability, the condition of the muscular wall of the stomach, and the early diagnosis determine the probable duration. If not relieved by appropriate treatment these patients get rapidly worse and fail from inanition; surgical intervention (gastro-enterostomy), on the other hand, may alter the whole course of the malady, and quickly bring about recovery even after advanced disease exists and after years of suffering.

The stenosis of luetic origin may improve under specific treatment, or else the newly formed scars which result from the effect of specific treatment upon the healing process may also increase the stenosis. Cancerous stenoses, of course, run a progressively downward and usually a rapid course unless removal of the neoplasm is carried out. Under rare conditions, they improve markedly for a time, either because the pylorus is reopened through breaking down of the obstructing cancerous mass, or because of the effects of general treatment.

The occurrence of gastritis and intestinal disease lengthens the duration of the malady and adds to the difficulties of cure. Relapses are very common in the idiopathic cases, and are usually dependent on indiscretions of diet or excesses in daily routine. Persistence in the exacting treatment is by no means easy, and the tendency to relax in care makes it difficult for patients to lead a model life of the kind required for permanent cure.

**Prognosis.**—In the early stages of gastrectasis one should carefully guard against a too definite assurance as to the cause and probable outcome. The two features which govern the prognosis are the cause and the possibility of its removal. Cures are possible in idiopathic cases that are even advanced, provided the wall of the stomach is not permanently damaged and the general condition of the patient capable of improvement. Gastropptosis renders these cases much more difficult of cure. Early cases are of course always amenable to cure if the proper treatment be employed and conscientiously carried out. The normal amount of urine, the lessened degree of thirst, the good condition of the musculature, and possibility of obtaining suitable diet are all favorable features. The onset of tetany is a serious complication and one of grave omen. Relapses are common and due recognition of their frequency is important in dealing with questions of prognosis. In obstructive cases the cure is always possible, except in malignant disease, for the possibility of surgical intervention, when a new opening may be made to short-circuit the passage, renders a benign stenosis of no importance in itself.

**Prophylaxis.**—Proper hygiene, diet, and mode of life are essential to the prevention of pure gastrectasis from atony of the stomach, as is also moderation in the use of food and drink. Special care in debilitated states, as regards diet, exercise, and habits, must also be carefully remembered, and one should avoid the previously mentioned causes of idiopathic dilatation.

**Treatment.**—A detailed diagnosis as to the nature of the gastrectasis is essential to rational *treatment*, which should be based on (a) the etiology as regards food, drink, and habits, and (b) the social state, history, family history, previous diseases, and conditions of the viscera. In all patients with motor insufficiency certain general rules apply, no matter what the cause or underlying condition may be. The stomach must be as far as possible emptied within the normal time, and stagnation and retention of food avoided. Food must be administered of a kind which, as regards quantity and quality, will not excessively burden the stomach. The motor power being weak, one must aid its activity by avoiding unnecessary effort on the part of the gastric muscle, while fermentation must be avoided or reduced to a minimum. Where pyloric stenosis exists surgical intervention must be carefully considered. In the benign cases it is often curative.

**Diet.**—The main objects are as follows: (a) To supply sufficient nutriment in an easily assimilable form, (b) to avoid over-burdening the weakened stomach with bulky foods, (c) to avoid fermentation and retention of foods, (d) to give foods of such kinds and in such a way as to assist their early propulsion into the intestines where the chief digestive function is carried on, and (e) to supply enough fluid to the body to fulfil the requirements of tissue thirst. These results are best obtained by giving frequent small meals, six small meals daily rather than three of ordinary amount. Food must be given either in soupy form, or as dry, solid food in a finely divided form. It must be taken slowly and well masticated; for this reason the teeth must be kept in good condition. The patients must rest before and after food, preferably in a recumbent position, on the right side. Occasionally lavage assists materially. This principle depends on the evidence given some years ago by von Mering, that water is not absorbed in the stomach, so that its propulsion into the intestine is necessary for its usefulness to the tissues.

In any case much fluid should be avoided, no matter how great may be its nutritive value, for gastrectasis has been well called dyspepsia of fluids. Whatever of fluids be taken they should be sipped slowly. Milk, being one of the most perfect foods, is also one of the most suitable in gastrectasis. It is well to add some cereal to it, *e. g.*, barley, rice, oatmeal, etc., or one of the numerous concentrated albuminous foods. One may add cream or make a custard. Milk is often distasteful to patients who suffer from retention of food, and for this reason any ordinary flavoring extract may be added to aid in its administration. The addition of lime water or brandy may be desired and may effect the same purpose. Bouillon with eggs makes an excellent form of concentrated nourishment, and is usually readily assimilated; so also are meat juices and meat jellies. The dry foods and those more solid should be prepared in a finely divided form, especially the meats and vegetables.

Whatever meats are used should be chopped up and well masticated. Scraped raw beef, tender roast beef or fillet, thinly sliced smoked ham, oysters, and sweetbreads are often well borne, as also chicken, pigeon, tender mutton, and white fish of various kinds. Vegetables must be mashed or in pureé form. Only the less coarse varieties and those with

least cellulose should be employed. Pureés of potatoes, peas, spinach, asparagus-tops, or cauliflower can usually be taken with ease. Bread may be given, preferably white stale bread, or toasted, or one may use rusks and unsweetened biscuits. Fats, notably milk fat, are good, especially with the addition of HCl. Alcohol is of value only when weakness is great and small quantities of stimulant are necessary. It should be remembered that although absorption occurs in the stomach, the alcohol at the same time induces an increased secretion of water into the stomach. Malt extract in small amounts may aid the appetite.

*To some extent the diet must depend on the results of gastric analysis.* With *subacidity*, cereals are preferred rather than albumins, and whatever meats are used should be finely divided before eating. White meats are preferable, and dry white fish is usually well borne. Vegetables, even though better taken than proteins, must be finely divided and given in limited amount. In these cases the use of drinking water to which a little diluted HCl has been added is often beneficial; it should be sipped slowly after food. With *hyperacidity* one should select mainly albuminous foods, meat, milk, eggs, and fats in moderate amount, of which butter is the most easily borne. Starches should be carefully restricted, although rusks and dry toast are suitable. Sweets should either be much limited or altogether avoided. Fluids are more tolerated than in subacidity, especially the still alkaline waters. *Saline enemata* are often most useful to relieve the tissue thirst in idiopathic dilatation.

Of *mechanical measures* the most important is thorough lavage of the stomach. This is indispensable in the medical treatment of motor insufficiency if that condition be at all marked. In the mild cases it may not be required, although it often affords great relief. It is not merely a form of symptomatic treatment, but is even curative in the early cases. As a rule, however, early mild cases merely require strict attention to diet and daily regimen to effect a cure. One must judge according to the individual case how much lavage is necessary. In the moderately severe cases the stomach is never empty during the course of the day, food being retained until the subsequent meal, but the stomach empties itself during the night. In such cases a careful lavage given before the evening meal does good by removing the fermenting products of the day's feeding, and a small appropriate meal taken thereafter on an empty and cleaned stomach has a good opportunity for absorption with the patient at rest for the succeeding ten hours.

In the very severe cases when food remains in the stomach over night, and has not been propelled into the intestine by early morning, lavage is still more imperative, and in the most extreme forms it may be well to wash the stomach twice daily, in the early morning as well as in the evening. The essential is that the lavage be thorough, and that the return flow of water be finally quite clear. It may be necessary to wash out the stomach with the patient in various positions, standing and lying down. Much time and patience may be needed, and often an hour of lavage is required before the water returns perfectly clear. Lavage should not be left indiscriminately to the patient, but the physician does well in most cases to perform it in person or by a trained assistant.



Lukewarm water suffices for the purpose, although when much fermentation is present, salicylic acid solution (1 to 1000) may be used. How long should one keep up lavage? This must depend on the persistence of motor insufficiency. It should be done daily until we are sure the digestion is not delayed overnight. The lavage should be discontinued gradually, daily treatment giving place to one washing on alternate days, the condition of the contents deciding the subsequent frequency.

Other mechanical measures are of less importance, although often of benefit. Massage is beneficial in a general way, but should be used systematically, and under proper skilled direction. In extreme cases of gastrectasis it is not well to employ vigorous massage to the abdomen, for it is not supposed to benefit the muscle of the stomach directly, but assists more by increasing the general muscle tone, by improving the circulation, and aiding the nervous system. It also assists in obviating the chronic and often most persistent constipation. It should not be done until at least one and a half hours after any meal. When much fermentation exists, or where there are organic causes for the dilatation, it is well to avoid the upper abdomen and confine the treatment to the lower zone and to the general musculature elsewhere.

*Hydrotherapy* is of the greatest benefit; in fact, apart from lavage, there is no mechanical treatment so beneficial in gastrectasis. Warm shower douches gradually made colder, with the use either of the strong hose stream playing up and down the back, the use of the Scotch douche, the employment of salt rubs, or of douche massage give eminently satisfactory results. When hydropathic apparatus is not available, much benefit is gained from daily cold baths, followed by dry friction with a rough towel. The use of compresses over the stomach at night covered with oiled silk and a binder often gives great relief.

Bandages of a supporting nature, or proper-fitting corsets for women which support from the pelvis, are useful; such corsets are constricted about the hips, but are loose about the epigastrium and lower part of the thorax, thus affording room for breathing, and not allowing the stomach to be without support from below. These are especially useful when gastroptosis exists.

*Electricity* has merely a general value in the same way as has massage. Its direct local action is very dubious. Experiments on dogs have shown that faradism does not directly affect the gastric muscle, but causes contraction merely of the external abdominal muscles. Apart from this general effect, electricity, even if applied as intragastric faradism, is but another form of suggestive therapeutics. The same applies with even more truth to the use, or rather the abuse, of static electricity and high-frequency currents.

*Drugs* form the least satisfactory of all methods in the treatment of gastrectasis. No drug that is known can effectually contract the dilated organ or act with continuous benefit upon the gastric muscle. Strychnine is much used for this purpose, although but little evidence exists to prove that its value is other than as a general tonic. The drug therapy is purely a symptomatic one. When hypersecretion exists, relief is often obtained from atropine in small doses (gr.  $\frac{1}{100}$ ) at night, or if need be

in the morning as well. Alkalis have perhaps an indirect value in neutralizing an excess of acid, although, of course, they have no effect in diminishing the secretion. For subacidity the use of well-diluted HCl sipped in a tumbler slowly every few minutes after food seems to aid digestion, or at all events to give added comfort. The use of bitter vegetable tonics is much lauded. In moderately severe cases the writer has had beneficial results from the use of olive oil, in dessertspoonful doses after food, as was recommended by Cohnheim. This author, however, preferred its administration through the tube in doses of 200 to 500 cc. Antifermentatives can only be of use in the milder cases, but with marked prolonged retention their use can have but little effect. Probably salicylic acid is one of the most satisfactory.

*Constipation* requires varying treatment according to its degree of severity. In mild cases no drugs are required, and proper feeding, massage, exercise and perhaps occasional water enema will suffice. It is often useful to administer Rochelle or Sprudel salts in small doses in the early morning, after which the patient takes moderate exercise for a short time previous to breakfast. In any case drastic purgatives do harm, and only mildly acting drugs are to be recommended. Should these fail in the more severe forms of dilatation, reliance must be placed on enemata every other day. Daily evacuations are not necessary to health, and patients should be advised accordingly.

*Vomiting* should be controlled by proper diet and by lavage. When these are ineffectual, nutrient enemata should be administered, and in persistent cases it will be necessary to call for surgical intervention. For the thirst the proper use of saline rectal injections will aid, and the mouth should be frequently rinsed with some pleasant wash.

**Surgical.**—The indications for operative interference include three types of cases: (1) Acute cases when medical treatment has failed or is known to be useless, *e. g.*, with twisting of the duodenum. (2) Pyloric stenosis, whether for removal of adhesions, fibrous bands, tumors obstructing the orifice, external compression from any cause, or when relief is impossible unless one is enabled to create a new passage for the food. (3) Idiopathic dilatation without marked gastropnoia or general enteropnoia, when medical treatment has been unsuccessfully tried, and where, in consequence, the patient is losing in weight and strength from insufficient nutriment, or again, when the symptoms even though not grave, are sufficiently irksome to interfere with daily routine.

Two objects are to be attained: (1) To remove the cause; (2) to remove the results. The methods are: (1) Resection of the pylorus, pylorotomy. (2) Heineke's pyloroplasty. (3) Gastro-enterostomy. (4) Bircher's gastroplication, which reefs up the anterior wall and diminishes the size of the stomach. This latter was advocated by Keen, Weir, and Brandt. Eight of Bircher's ten cases did well. Gastro-enterostomy in uncomplicated cases has given excellent results. Enteropnoia is distinctly a contra-indication to surgical interference—and even mere gastropnoia, if at all marked, is not likely to permit of successful operation in cases of gastrectasis, even although the gastrohepatic omentum be shortened to aid in removing this complication.

## "CONGENITAL" HYPERTROPHIC STENOSIS OF THE PYLORUS

**Synonyms.**—Congenital pylorospasm; hyperemesis lactentium (M. Schmidt), infantile hypertrophic stenosis of pylorus.

**Pathology.**—Two distinct conditions seem to exist:

1. **Pylorospasm.**—This, without true hypertrophy, is described by Pfaunder in systolic and semisystolic stomachs, a pseudohypertrophy. The condition is often seen at operation and autopsy, for fixation of the muscle occurs during certain phases of digestion. Heubner and Freund share this view. These cases must be regarded in the light of mild types, of short, perhaps intermittent course, and not requiring surgical intervention because there is no permanent anatomical disturbance.

2. **True Hypertrophy.**—The pyloric ring is increased in size and thickness, owing to hypertrophy of the muscular fibres, chiefly the circular ones, although it is difficult to measure to what degree the longitudinal muscle shares in the increase. The swelling is sharply delineated at its duodenal end, but diminishes gradually toward the fundus. The mucous membrane is folded up and the submucosa is little, if at all, altered. The lumen is small. The stomach is dilated, and in cases of long standing often shows a diffuse hyperplasia of its muscle. The duodenum is empty. It is quite conceivable that all transitions may occur between mere spasm and true hypertrophy.

**Pathogenesis.**—The recent work of Cunningham, Stiles, and others has thrown much light on the anatomical condition. Normally, the stomach may be considered as an organ in which the pylorus is a distinct and separate portion, with a function both to expel and to retain food. The cylindrical canal, which is about 2 to 3 cm. long, is contracted at birth, and its lumen is obliterated by the folds of mucous membrane. The ring projects normally into the duodenum in a way similar to that in which the cervix protrudes into the vagina. The muscular fibres of the pylorus are so arranged that the circular ones, which surround the whole length of the canal, are to some degree antagonized by the longitudinal bundles, which as Cunningham shows are derived from the body of the stomach, and spread about, in gradually increasing numbers over the pylorus, and dipping even into the submucosa, aiding in relaxation of the sphincter. Between the circular fibres of the pylorus and those of the duodenum there is a dividing band of connective tissue. In the cadaver the pyloric canal is usually tightly closed, so also probably during life except during digestion, when it opens irregularly and intermittently. When pyloric stenosis exists, the whole canal is probably involved, and the changes are primary, while any lesions in the stomach elsewhere are secondary.

Other conditions of a mild nature, such as recover readily on medical treatment, may be regarded as due, in most instances, to obstruction of the pyloric lumen from swollen membrane or an inspissated mucous plug, a condition, too, that one might readily conceive to be associated with spasm. Such a case was described by Scholten, in which a true thickened membrane was observed at operation and at postmortem.



Doubtless the earlier observers had the correct view in regarding the condition as developmental hyperplasia of the pyloric muscle, a congenital redundancy, or prenatal overgrowth (Nicholl, Cautley, Ibrahim). The fact that the pylorus first appears in fetal life at the third month shows that enough time exists before birth for excessive growth, while the degree often found excludes the possibility of postnatal development. Sometimes when pyloric stenosis occurs as a congenital condition, other parts of the body show abnormalities, *e. g.*, there may be congenital atresia of the anus, and perhaps, as Stiles suggests, we have an analogous condition in incontinence of urine with overdistension of the bladder, overcoming finally the sphincter vesicae. Other analogous conditions are pathological dilatation and hypertrophy of the rectum. - Torkel, in 1905, cites an instance in which, on anatomical grounds, a proof exists of a congenital origin, aberrant embryonic tissue (Brunner's glands) being found amid the fully developed structures.

A nervous theory was advanced by Thomson and Still, according to which the condition was associated with disturbed coördination of the relaxing and contracting fibres of the pylorus, with increased irritability, and this latter whether originating during intra-uterine or extra-uterine life leads to spasm, and this spasm leads to hypertrophy—a hypertrophy from overwork. However, no proof exists of incoördination or of nervous derangement in fetal life. Nor are we sure that spasm causes the hypertrophy of the pylorus. If this were the case, the same spasms might be expected then from other conditions of irritability, *e. g.*, hyperacidity and faulty feeding, but such facts have not been shown to occur. Freund, however, regarded hyperchlorhydria as an important factor.

**Symptoms.**—The condition is more frequent than was supposed until recently. The infant, frequently the first-born and, as a coincidence, more often of the male sex, is healthy at birth; symptoms usually begin to show from the third to the sixth week, and very rarely as late as the fourth month. Very few cases are on record in which the symptoms began immediately after birth—a point of great importance in the diagnosis. Cases may go on to adult life and Bassler has described authentic instances. Digestive troubles of an intermittent type usher in the symptoms. The breast or the bottle is taken reluctantly no matter how careful the feeding, and the child is easily satisfied. When vomiting begins early, however, the appetite is often maintained in a striking way. *Vomiting* is the chief early sign, is explosive, and often copious according to the degree of retention. At first it seems unimportant, although no adequate cause is found; then its persistence rather than its frequency attracts the attention. Gastric analysis gives variable results.

**Signs.**—Constipation is the rule, requiring the use of enemata, or more rarely diarrhoea occurs with green, watery stools, containing mucus, and perhaps tarry from the presence of blood. The urine is diminished. Wasting is sometimes rapid, and there may be marked weakness, the result of the starvation, the condition resembling and often being mistaken for marasmus. The child is often in severe pain, with violent cramps and epigastric resistance, and cries out or whines; at other times it is quiet and dull.

*Dilatation*.—Sometimes the stomach region bulges if the organ be full, and the dilated viscus may be seen extending to the navel. Dilatation is often marked; in one of Henschell's cases the stomach held 400 cc. Heubner found the majority of cases with undistended stomach, which he attributed to the constant vomiting. Dilatation is perhaps more common with bottle-fed infants. *Visible peristalsis* is most marked in long-standing cases, although Sarvonat and Audry described it in a child aged two weeks. Probably when mere pyloric spasm exists, without true hypertrophy, there is much less peristalsis. It is an important sign when present, although not always found, and often only at long intervals especially after food. The *tumor* may be palpable, is sometimes lower than, and sometimes beneath the enlarged liver, as a hard cylindrical or spherical lump, the size of a filbert, which may even be felt to contract and to change in hardness during peristalsis.

**The Diagnosis of "Congenital" Hypertrophic Stenosis (not Pylorospasm).**—The symptom complex gives the clue. (1) The time of onset and the age; symptoms develop in early infancy, but not immediately after birth. (2) The vomiting, which is persistent and forcible, occurs always after meals, but also regardless of feeding in healthy children. (The vomitus does not contain bile.) (3) The absence of milky stools. (4) The visible peristalsis. (5) The tumor, which is palpable as a finger-like mass, and movable downward. It is not always to be felt, as it sometimes lies under the liver, in which case one must diagnose by exclusion and by a careful experimenting with food. (6) The dilated stomach. (7) The crying from hunger and pain. (8) The emaciation.

Congenital hypertrophic stenosis is to be distinguished from (1) *simple regurgitation* in which the above symptom-complex is absent. (2) *Stenosis of the duodenum*; kinking from shortened ligaments, adhesions, etc. (3) *Tumors* near the duodenum, such as enlarged glands narrowing the lumen by pressure from without. (4) *Congenital atresia of the pylorus*, which is a rare condition due to developmental error and rapidly fatal. It is therefore incompatible with life, unless relieved by operation. Vomiting occurs immediately after birth, even if food is withheld, or in other cases as soon as this is given. (5) *Malformations and atresia of the small intestines*. There is bile in the vomitus and the duration is short, at most a week. Sometimes an atresia occurs at the pylorus or in the duodenum, and is incomplete at first, so that the failure of health is more gradual, and the stomach may be hypertrophied in consequence. (6) *Gastritis*. (7) Simple vomiting and constipation from faulty feeding. (8) *Habit vomiting*. (9) *Pylorospasm* due to faulty feeding. Here the signs and symptoms are similar, but milder, as a rule; there is less visible peristalsis and the contracted nodule is usually smaller than the tumor of true stenosis. The condition, too, is more amenable to treatment.

**Prognosis.**—This depends to a large extent upon one's ideas as to what is meant by the term pyloric stenosis. Wherever the symptoms are due to pylorospasm or to obstruction from a swollen mucosa and plugs or mucus, the patients recover on a careful diet and rational therapy. Both mild and severe cases occur, the latter often producing

extensive gastrectasis. True hypertrophic stenoses are much more serious, and in the grave cases the result depends upon surgical treatment being undertaken early. To wait too long is a grave error, and yet experience shows in many instances that proper variation of the food often produces excellent results and rapid cures. Koplik's cases bear out the importance of suitable diet. When dilatation and marasmus exist, the prognosis is more serious (Cautley). The milder cases have less hypertrophy and obstruction, and may get well with lavage and diet, or else may pass into a mild chronic state with gastritis and ultimately die from marasmus. Other cases may terminate later in life with dilatation and hypertrophic stenosis, and perhaps originate some of the instances seen in adults. That congenital stenosis of the pylorus in adult life is common, as held by some surgeons, is scarcely yet proved.

**Treatment.**—In the early stages the diagnosis is usually doubtful, and the patient should be subjected to medical treatment under careful observation, to determine whether one is dealing with stenosis from mere spasm, temporary obstruction, or with a true hypertrophic condition.

**Dietetic.**—Careful feeding with non-irritating food and rest after feeding is the main thing. If the child is being nursed, the breast feedings should be regulated; if artificially fed, a wet-nurse may be employed, or the simplest kind of food, as whey, albumin water, peptonized milk, and raw meat juice, in small amounts, may be used. Fats should be very limited in quantity, these being the last to leave the stomach, and for that reason a milk with a low fat percentage should be selected. Heubner recommends feeding every three hours, as much as they care to take, letting them vomit, and applies poultices three times daily for two hours, changing every half hour. Batten suggested nasal feeding, but this is of doubtful value. The infant should be weighed from time to time to estimate the value of the feeding.

**Mechanical.**—Lavage is of great benefit, relieving the vomiting and distress, keeping up the appetite and helping nutrition indirectly, but lavage does not cure the condition and may easily deceive the clinician as to its true nature. Saline injections per rectum may be useful.

**Medicinal.**—Various remedies are suggested, the main objects being sedative:  $\frac{1}{15}$  of a drop of tincture of opium with a few drops of tincture of valerian (Heubner); or  $\frac{1}{100}$  gr. of cocaine, or, better still, *atropine* in small doses will relieve spasm by its action on the muscle tone. Alkalis by neutralizing the excess of HCl help to relax the spasm. They should be given after feeding. Koplik adds citrate of soda to the food.

**General Medical Directions.**—One must watch the weight, but need not expect a gain at once. If after a few days there is marked loss of flesh, weakness, tetany, or convulsions, operation is indicated. If there are persistent vomiting, progressive emaciation, visible peristalsis, and absence of feces in the stools, the indications for operative treatment are obvious.

**Operative Measures.**—Just so soon as it is wise to operate this should be done without delay. The difficulty is to know clearly the surgical indications when a true stenosis is not so obvious. Divulsion if possible is preferable, either by means of Einhorn's rubber bag or Sippy's method.



The operative methods employed are—divulsion, gastro-enterostomy, pyloroplasty, and pylorotomy, the choice being a matter of surgical opinion, and as yet the statistics are unreliable.

### CIRRHOSIS OF THE STOMACH

**Definition.**—This may be defined as a non-malignant, slowly developing, and progressive affection of the stomach, characterized by diffuse or circumscribed increase in the connective tissue, involving chiefly the submucosa, and to a less extent the other layers, and sometimes extending to the connective tissue in the parts bordering upon the stomach. The definition excludes all cases of scirrhus cancer.

**Nomenclature.**—Although the condition has been recognized for more than two centuries, there have been so many views as to its underlying cause and its real nature that the synonyms for the disease are very numerous; *e. g.*, chronic interstitial gastritis; sclerosis of the stomach; fibroid induration; stenosing gastritis (Boas); fusocellular sarcoma (Lyonnet); plastic linitis (Brinton). This last term seems to have been that generally adopted, and certainly the French writers have done much to perpetuate its use. The nomenclature is probably also confused through an apparently unnecessary mingling of various conditions, each of which has a different cause. The names mostly describe the nature, situation, and extent of the lesion, the anatomical change being the same.

**Historical.**—We are indebted to Andral (1835) for the first accurate description of the condition and its differentiation from cancer, though descriptions occur as far back as the seventeenth century. Rokitansky, in 1859, maintained that submucous hypertrophies of the stomach belong in reality to the group of fibroid cancers. Brinton, however, two or three years later, gave to the condition the most used names “cirrhosis of the stomach,” and “plastic linitis,” thus assuring to it a clinical and anatomical distinctiveness. He classified it, not in the category of gastritis, because he held that the mucous membrane was never affected at the onset, and, indeed, was often quite intact; neither was it a hypertrophy, for often in the midst of new tissue much atrophy exists, but rather he regarded it as a cirrhotic inflammation, and not a pure sclerosis, which latter term applies merely to the last stages of the disease. Brinton recognized both its resemblances to and its dissimilarity from cancer, and admitted the difficulty of satisfactory classification owing to the insufficiency of data.

Among the most important papers which have appeared in connection with the subject was that of Hanot and Gombault, in 1882, a contribution of special value in view of the careful microscopic examination made in almost serial sections of the diseased tissue. The lesions were most marked at the pylorus and lesser curvature, and there was much invasion of the neighboring tissues, thus creating a callous retroperitonitis; but nowhere could they find either macroscopic or microscopic evidences of a malignant origin. Such, too, was the experience of Tourlet, who discussed the whole subject some ten years later, and who concluded

from his own observations and from analyses of others that the disease was not cancerous. Nevertheless, to Bret and Paviot cirrhosis of the stomach is merely a cancer with cells which are metatypical in the stomach, and the real nature of which is only seen in those rare instances where one finds in the generalized process the typical gastric epithelial cells which came originally from the stomach lesion. Garret, a pupil of Bard, seemed to regard the condition as of the nature of a fusicellular sarcoma. Still more recently Jonnesco and Grossman insist on the benign character of the lesions (1908).

**Pathogenesis.**—Diverse as the views are of the nature of this condition, and uncertain as is still its origin, many of the theories advocated may be readily refuted by an analysis of the reported cases. That it is not essentially an advanced stage of chronic gastritis, for instance, is demonstrated by the comparative infrequency of typical inflammatory lesions of the mucosa, which in so many cases appears quite unaffected. The same holds true of the theory of Fenwick, for primary atrophy is by no means a constant or even frequent lesion. Arteriosclerosis and senile changes do not again explain many cases occurring in young subjects, devoid of the manifestations of senile disease. Nor, again, is tuberculosis anything but a rare accompaniment and obviously a mere coincident. The occasional presence of ulcer, as described by Formad, Hoche, and others, does not certainly explain the origin of those advanced cases of linitis in which, in spite of the extensive disease of the submucosa, the overlying mucous membrane was intact, and showed not the slightest evidence of either recent or healed ulceration. Alexis Thompson described in 1913, a series of cases with fibromatosis of the gastric wall, non-malignant and not necessarily originating from ulcers. It is, however, more difficult to decide whether the theory of its cancerous origin is or is not applicable to all cases. There is no doubt that clinically the features are, as a rule, not usually identified with cancer of the stomach, *e. g.*, the long duration, the slow cachexia, the long remissions, the character of the emesis, etc.; furthermore, the presence of the oblong tumor, cylindrical, regular, unyielding, with an abscess of secondary invasion or metastases, all point to a condition of chronic inflammation rather than that of carcinoma.

Conclusions from the observations hitherto made would lead one to believe that plastic linitis is an interstitial overgrowth, chiefly in the submucosa, with or without muscular hypertrophy, in some cases primary from an unknown cause, in others secondary, perhaps to ulcer or to cancer, or to a cancerous degeneration of an ulcer; and at times perhaps associated etiologically with other irritating conditions such as might anywhere in the body favor the overgrowth of connective tissue.

*Sex* seems to have no influence in its causation. Trauma, through compression of the epigastrium from occupation, is mentioned by Hare, Schacher, and also by Snellen as a possible factor. There is no proof that alcohol induces the linitis, nor does the frequent association of this poison with chronic gastritis bring it into any nearer relation to the other malady. Moreover, in many of the cases described there is an

assured absence of an alcoholic history. Syphilis has been mentioned as a possible cause, although where this is present one may be said to be dealing with a specific disease by itself and not with plastic linitis.

**Pathology.**—The lesions which are essentially sclerotic and hypertrophic vary in their location, in the extent and multiplicity of their various foci, and in the degree of invasion of other structures. The typical lesion usually described is that found in the diffuse variety. The stomach itself is either of normal size or contracted. It may be freely movable, fixed in the epigastrium, or pulled up underneath the liver by firm adhesions to the gastrohepatic omentum. While at times it is universally surrounded by adhesions, these are usually most firm at the splenic end. They may be so firm and extensive as to cause intimate attachment to any of the neighboring organs and tissues, to which the same process may likewise extend. The capacity of the stomach is usually diminished in these diffuse cases, and it may not contain more than 150 cc. Dilatation occurs, as a rule, only when the pylorus is involved. Externally the organ has a grayish appearance, with a curious opacity due to the overlying peritoneum. It is oval, irregularly ovoid, or cylindrical in shape, resembling in size and form a thickened transverse colon. Its consistency is firm, in parts almost cartilaginous, but with the elasticity and resiliency of a large artery. When removed from the body and placed upon the table its shape is retained because of the thick, firm walls. The cut surface is unevenly thick, and may be in some places twenty times greater than normal; although in most instances the average thickness has been 2 to 2.5 cm. Usually the greatest thickness occurs at the pylorus, the hypertrophy gradually diminishing as one gets farther away from the outlet of the stomach. More rarely the cardia is chiefly involved, or it may happen that several portions are separately diseased, the intervening tissues remaining comparatively normal. Everywhere the cut surface has a fibrous, pearly grayish appearance and the individual layers of the stomach are readily recognized.

The *mucosa* is often normal in appearance and structure, or slightly thickened and firmer than normal, and in some cases can be lifted off from the submucosa. The thickness is diffuse or patchy, and in a few instances areas of atrophy are also seen, with pale or reddish color or pigmentation. It may be smooth or rough, the surface being sometimes thickly granular with excrescences. Sometimes a few polypi are seen, and there may be erosions, ascribed by Pillet to vascular obliteration due to fibrous constriction. The *submucosa* presents the greatest hypertrophy and thickness. Its tissue is dense and firm, its color grayish-white, and the fibrous strands running through and from it in all directions traverse the underlying muscle tissue so as to form a network about the individual bundles (hence the name "linitis").

The *muscularis* is likewise thickened from true hypertrophy of the muscle, as well as an increase in the connective tissue among its bundles. The fibrous tissue may finally invade even the subserous cellular tissue, so frequently, indeed, that Brinton regarded this layer as the site of origin. The peritoneum may or may not be involved; in the case of



Hanot and Gombault so great was the involvement of peritoneum as to render it worthy of a special title—*rétropéritonite calleuse*. There was chronic inflammation, with thickening, induration, retraction of the stomach, and fixation of the organ. Amid the adhesions which involve the gastrohepatic omentum, the great omentum, and the gastrosplenic ligament, obliteration of the common duct and the portal vein has occurred, and even an obstructive biliary cirrhosis. The visceral capsules may be thickened (liver and spleen) and these organs themselves sclerosed or atrophied. Even the intestines are sometimes thickened (more especially the transverse colon), and their caliber diminished even to complete obstruction. Simultaneous involvement of the cecum has been mentioned.

The *lymphatics* of the mesentery are frequently seen to be dilated, sometimes so markedly as to suggest that the lymphatic obliteration was the primary cause of the condition (Bouveret, Tourlet). The *glands* are almost invariably small, although their cut surface may show an interstitial increase similar to that seen in the submucosa.

**Histology.**—The mucosa shows either a normal condition or the minute lesions of a chronic productive or atrophic gastritis. The glandular structures may be displaced and the development of fibrous tissue may cause constrictions and cystic dilatations of the tubules, or else may have caused the gland structures to entirely disappear. In a case mentioned by Osler the mucosa was smooth without any trace of glandular elements—a distinct sclerosis of the mucous membrane itself with atrophy. The lymphoid nodes are sometimes proliferated. The submucosa, which is much thickened by strands of fibrous tissue densely arranged, and forming a network, may be at times most abundantly gathered around the bloodvessels. And the muscularis, which is normal in some places, is in others like an irregular checker-board traversed by intersecting lines of fibrous tissue. The subserous layer exists in various stages of progressive inflammation, and the peritoneum itself may show increased connective tissue, and more or less destruction of the endothelial cells.

The *circumscribed form*, of which the commonest and most typical lesion is the “hypertrophic stenosis of the pylorus,” shows anatomical lesions of a similar nature, although, as a rule, there is dilatation of the organ rather than contraction, and the muscle tissue itself gradually degenerates. Habershon’s fibroid disease of the pylorus and Boas’ hypertrophic stenosing gastritis are the synonyms. The delimitation toward the stomach itself is usually gradual, while toward the duodenum it is much more sharply defined. The cases of congenital hypertrophic stenosis of the pylorus may sometimes belong to this category, although their origin is more of the nature of a developmental morbidity than of an inflammation. Of the other sites of localization the cardia has already been mentioned, and Formad’s case, in which the greatest thickening was at that orifice, is worthy of special mention. An ulcer existed in the posterior wall near the cardia, the floor of which was formed by splenic tissue and the peritoneal coat of the transverse colon. The stomach was contracted and held less than 150 cc.

**Symptoms.**—The onset is insidious, and the early development slow, gradual, and by no means easily determined. The early symptoms correspond in most particulars to those of chronic gastritis, and there are vague symptoms of indigestion, with a fickle appetite and usually anorexia, a sense of heaviness after meals, and later vomiting of mucus or of partially digested foodstuffs. In the early stage pain is moderate or entirely absent, and rarely so severe as to suggest ulceration. For one or more years these milder symptoms, which are usually slowly progressive, or else with occasional long periods of remission, are gradually superseded by signs that indicate a more serious disease. The pains, which at first were insignificant, become more constant, of a dragging nature, sometimes spontaneous, sometimes only excited by food. They may extend from the epigastrium to the back, and are usually increased by pressure. Nausea, eructations of gas, and vomiting of liquid gastric contents accompany the pain, which is usually relieved by free emesis. The *vomiting*, which is always digestive in time, appears sometimes at once after meals, as though from an involvement of the œsophagus, and Roux has drawn special attention to the diagnostic importance of this symptom as suggesting gastric intolerance because of the rigid contracted cavity. When the chief lesion is at the cardia, regurgitation of food or mucus would be a common sign, but in the commoner diffuse cases the vomiting appears one to two hours after meals. It is most continuous in the severe cases, and if stenosis of the pylorus be present there will be signs of retention. In about 20 per cent. of the cases slight hematemesis is noted, but there is never much bleeding because there is rarely ulceration. For the same reason obvious melena is uncommon. The increasing limited capacity of the stomach for food is an important symptom. The intestines are not commonly involved, but sometimes the bowels are irregular and there may be a mucous enteritis. The general appearance of the patients may vary; while, as a rule, some pallor is conspicuous, the patient has lost flesh, and has become somewhat cachectic, yet at other times, both the nutrition and the color are well preserved, a circumstance to which Trousseau has drawn special attention.

In the gastric contents, the HCl is variable, often absent, and lactic acid is commonly present.

Examination of the abdomen in uncomplicated cases may show some retraction of the epigastrium, or a mass, more or less localized, may be seen prominently beneath the abdominal wall or moving with respiration. Peristalsis may be visible. Palpation demonstrates, usually, a diffuse resistance in the epigastrium, not always marked, especially if the contracted stomach be drawn up and fixed beneath the liver. At other times a hard oblong transverse tumor may be felt in the epigastrium, and extending to the left false ribs, or again only in the neighborhood of the pylorus. The *mobility* of the tumor varies according to its site and the nature and extent of any adhesion present. It has been mistaken for a movable spleen and for the transverse colon. Trousseau has drawn attention to the sensation of grating conveyed to the palpating hand on deep respiration. As time progresses, the condition may extend beyond the stomach to the peritoneum and the surrounding viscera.

Ascites may develop, make palpation difficult, and conceal the real underlying cause; or the symptoms may change to those of intestinal obstruction, in which to the conditions of cachexia and anasarca may be added persistent and uncontrollable vomiting until death follows from asthenia. Jaundice is rare in these cases, and apparently due only to constriction of the common bile duct from adhesions. When the cardiac orifice is mainly involved, so that constriction occurs, the process is more rapid and the fatal termination induced through starvation and inanition. Rapid emaciation, dysphagia, regurgitation of mucus and food are the characteristic features. When typical hypertrophic stenosis of the pylorus is present the signs are those of a benign stenosis. To the primary digestive symptoms are added the slow development of the affection, the marked emesis, with is digestive, infrequent, and small in amount at first, and later less often but more abundant; later come the signs of marked motor insufficiency with constipation, great thirst, and hunger, diminution in the quantity of urine, localized pain, visible peristalsis, perhaps a visible tumor, rapid emaciation, and death from inanition.

**Course.**—Chronicity is the characteristic feature, and although Bouveret's case lasted apparently only twenty months from the onset, this is much shorter than the average duration. Tourlet's patient suffered seven to eight years before operation, and the average is perhaps ten to fifteen years. No general rule can be made, for the duration depends on the variety of the lesion. Circumscribed cases not obstructing an orifice will naturally last much longer than those which are localized at the pylorus, or still shorter time if at the cardia. The diffuse cases will be of still shorter duration than those confined to the pylorus, and where peritonitis, ascites, and adhesions supervene, the course is rapidly and progressively downward.

**Diagnosis.**—This has rarely been made during life. When, even at autopsy, it is so difficult to make an anatomical diagnosis, one can scarcely expect that the clinical diagnosis would be easy. While the uncomplicated cases are difficult to determine, still more do the cases with complications lack ready means of diagnosis. The chief features are the long duration, the slow cachexia, the limited capacity of the stomach, and its intolerance of much food at any one time, the absence of hematemesis or melena, the presence of an oblong cylindrical tumor in the epigastrium in patients in whom the history and physical signs present neither the local evidence of carcinoma, metastases, or any signs of generalization. Plastic linitis has frequently been mistaken for cancer of the stomach, for portal cirrhosis, for obstructive biliary cirrhosis and simple chronic or tuberculous peritonitis. When pyloric stenosis is present one considers the possible presence of an old gastric ulcer and consequent perigastritis, and for the elucidation one trusts to the past history. Syphilis rarely presents similar symptoms; as a rule, the lesion presents mere strands of fibrous tissue, and gummata are uncommon. Much interest attaches to Einhorn's case, as reported by Brissaud, in which a large tumor, the size of a pigeon's egg, disappeared in a few weeks under antiluetic treatment. Deguy, in 1896, described his case



in which, for the first time, a diagnosis was made during life, and subsequently confirmed at autopsy. McCrae reported a similar experience from Osler's clinic.

**Treatment.**—The rational treatment is essentially surgical. Medically there are but two considerations: in the early stage to treat the condition as in chronic gastritis, and later, when stenosis exists, to employ palliative treatment until the more radical cure is attempted by surgical measures. Gastro-enterostomy as a mere palliative operation has been found successful, but where possible, a removal of the diseased tissue, in view of the possible cancerous nature of the affection, is the one thoroughly scientific treatment worthy of consideration—for the localized condition, pylorotomy, and for the diffuse lesion, total resection. Mauclaire and also Terrier have recorded cases in which an apparent cure followed exploratory laparotomy, and Roux records an interesting case in which the patient was well three and one-half years after operation (anterior gastro-enterostomy). Total resection was performed by Gayet and Patel (1904) for a linitis of definite malignant origin, this being probably the first operation of its kind for this condition.

### HEMATEMESIS

**Synonyms.**—Gastrohemorrhagia; vomitus cruentus.

**Definition.**—Hematemesis is a vomiting of blood—regardless of its origin—and it must not be confounded with “gastrorrhagia,” for the blood vomited in hematemesis may come from other sources than the stomach itself. It is merely a symptom, to be referred not only to the stomach itself, but also possibly to conditions in structures contiguous to that organ. It is much more common than is usually recognized, probably because spectroscopic, microscopic, or chemical aids are not usually employed to reveal the presence of blood when not in macroscopic quantity. Certain minute hemorrhages more often go unrecognized than is usually believed, and in this way the early manifestations of disease remain undetected.

There may be no anatomical lesions (diapedesis), as in Lancereaux's supposed neuropathic hemorrhage occurring in gouty, nervous, or rheumatic individuals; or the lesion may be so minute as to escape detection even although the hemorrhage be very copious. Such conditions often arise from a general oozing from various portions of the mucous membrane, and in some cases the blood streams forth from a wide surface of the mucosa. More often the lesion is obvious (rhesis), and gross anatomical disturbance, such as ulcer, cancer, or phlegmon, explains its origin.

**Etiology.**—The bleeding may be (1) gastric, or (2) extragastric.

1. **Gastric Bleeding.**—Gastric bleeding may be from *local* or *general* causes. *Local* causes may be *direct* or *indirect*.

*Direct Local Causes.*—Among these are: Ulcers simple, round, tuberculous, typhoidal, diphtheritic, septic, etc.; varices, and miliary aneurisms, perhaps associated with arteriosclerosis; gastritis, simple, acute, chronic, phlegmonous, or toxic; cancer and trauma. The trauma may

be direct or indirect, and the causes physical and chemical. Physical causes, *e. g.*, foreign bodies; the strain of vomiting; injury from the stomach tube; stretching from distension by CO<sub>2</sub>. Chemical causes, as poisons, purgatives, emetics with degeneration of the mucous membrane, fatty, hyaline, or amyloid; and postoperative hematemesis, as yet ill-understood.

*Indirect Local Causes.*—Portal obstruction in cirrhosis of the liver, syphilis of the liver, atrophy, pressure on the portal vein, portal thrombosis (of these cases 80 per cent. are œsophageal in origin). Thoracic disease with circulatory obstruction, emphysema, chronic pleurisy, fibroid lung, and organic heart disease. Splenic enlargement, as in splenic anemia, etc.

*General Causes.*—In these hemorrhage occurs from various mucous membranes as well as from the gastric. The conditions are many: sepsis (with or without signs of local lesion); the exanthemata (hemorrhagic forms) and other fevers such as typhoid; hematemesis neonatorum perhaps belongs to this group; autotoxic states, uremia, cholemia, etc.; blood dyscrasias and diseases, hemophilia, purpura, scurvy, pernicious anemia, leukemia, etc., possibly degeneration of vessels and capillaries, or emboli with hemorrhagic infarctions or infected thrombi; neuropathies, epilepsy, tabes, general paresis, hysteria, and meningitis, in all of which the hemorrhages may be vasomotor in origin; vicarious menstruation and burns. Debove and Coutois-Suffit attribute these unexplained hemorrhages without discernible lesions to abdominal congestion due to depressor nerves acting on arterial tension, as has been declared possible by Ludwig and Cyon.

2. **Extragastric Bleeding.**—Apart from the hemorrhages which arise in the œsophagus from varices, etc., the blood may come from abscesses contiguous to the stomach bursting into that organ; or ulcers and fistulæ may open up a suppurating tract into the stomach and cause hematemesis. Vertebral caries or aneurism of the abdominal aorta or cœliac axis may perforate the stomach and cause hematemesis.

**Age and Sex.**—The age at which hematemesis occurs is usually from fifteen to forty; it is rare in infants. It is probably more common in women.

**Pathology.**—The originating cause will in large part determine the nature of the general changes, *e. g.*, cachexia in cancer, cloudy swelling in sepsis, etc. The mucous membrane of the gastro-intestinal tract is usually pale, and about the seat of the hemorrhage there will be the remains of blood more or less tarry. The clot formed varies in appearance. If there be little blood and gradual oozing one gets a chocolate or coffee-ground appearance perhaps, with black specks like powder sprinkled through the contents, or a diffuse bloody, or darkly stained fluid. At the seat of the hemorrhage one may find eroded vessels, and sometimes an imperfect clot formation. The opening is often very difficult or impossible to find or only evident after injection from the main vascular arrangement.

**Symptoms.**—These depend chiefly on the amount of blood poured out and the rapidity with which it flows. Sometimes gastric hemorrhage is

latent, especially when the amount is small, and the blood must then be detected in the vomitus or feces (occult). At other times the blood is not vomited even when very copious, and the patient may even die with no other signs than those of internal hemorrhage. In true hematemesis the blood, however, is vomited and may be large (up to two liters) or small in quantity. When small in amount it is usually mixed with mucus and food and appears either as minute specks or as streaks mixed with the other gastric contents. Its color depends upon its amount and the time in the stomach. The blood of minute hemorrhages is most easily transformed in color. When fresh, the color is bright and the blood cells are unchanged. When for some time in the stomach, the blood is dark and the oxyhemoglobin is changed to hematin, resembling coffee-grounds. Experiment has shown that if 50 cc. of blood reach the stomach and remain in it for five minutes, the red cells become altered and the color already much darker than normal. Microscopically one sees cells more or less broken down and blood pigment. Sometimes, again, there is much dark-red clot with an acid reaction.

The patient may have a sense of warmth in the epigastrium and along the œsophagus; sometimes an abnormal pulsation with fulness is felt in the abdomen. Pain is frequently felt in the epigastrium for some time before hemorrhage, and may cease when this occurs. If quickly vomited, the blood may come not only through the mouth, but from the nose, and may get into the air passages and cause coughing. As a rule, hematemesis is accompanied by great anxiety and fear of death. The general signs of hemorrhage are present—pallor, faintness, dizziness, ringing in the ears, specks before the eyes, dimness of vision, cramps in the thighs and calves and perhaps clonic spasms, cedematous swellings over the smaller bones and eyelids, drowsiness, insomnia at night; the pulse is often dicrotic, anemic systolic murmurs are heard over the heart, and a venous hum over the large vessels. The blood picture is that of a secondary anemia. Fever is present, especially if the intestines have contained much blood, because absorption occurs; on this account the temperature is not infrequently reduced by purgative treatment. Recovery is sometimes rapid, at other times very slow, because bleeding from the vessels may be often repeated and small in quantity.

**Diagnosis.**—When hematemesis has occurred one must consider the following questions: (1) Does the vomitus really contain blood? (2) If so, is it from the digestive tract? (3) Is it gastric in origin, and if so, does it come from near the cardiac end, from the duodenum, or from the stomach proper? (4) What is the etiological and anatomical lesion? (5) What vessel is affected? (6) Is it amenable to medical treatment, or, if not, is it accessible to operation?

Hematemesis is so often latent or unrecognized that one must make careful observations both as regards the previous gastric history and the present state of the abdomen and gastric contents or vomitus. Not infrequently there is a fulminating gastrorrhagia, in which no blood is vomited and the diagnosis is made from the general sensations and symptoms of hemorrhage and the previous history of gastric disease. Even when very copious it may not be evacuated and the patient may



die with merely the signs of internal hemorrhage, or vomiting may be delayed for some time, or the blood may appear only in the stools.

1. *Is Blood Really Present in the Vomitus?*—It not infrequently happens, both with patients and physicians, that a faulty diagnosis is made because the food previously taken may resemble blood, *e. g.*, red wine, cherries, cranberries, red cabbage, red turnips, red sausages, coffee, and cinnamon. Pseudohematemesis may be associated with various preparations of iron or bismuth; the bismuth crystals, moreover, under the microscope, resemble to some extent those of hematin. In doubtful cases one should always examine microscopically for blood cells or blood pigment, and where doubt still exists, test with the spectroscope or by chemical means, to prove the presence of occult hemorrhages.

2. *Is the Blood from the Digestive Tract?*—The blood may not be from the digestive tract at all, but from hemoptysis, epistaxis, or from a ruptured aneurism. To differentiate from hemoptysis one must remember that in hematemesis the blood is dark-red in color, usually resembling venous blood; that it contains no air, has usually an acid reaction from contact with the gastric juice; that it is mixed with food; that it is vomited, not coughed; and it does not contain tubercle bacilli, for tuberculous ulcers of the stomach are extremely rare; and lastly, local findings in the lungs are absent, while those in the stomach are often obvious; or there may be signs of a heart lesion, the possible cause of hemorrhagic infarction of the lungs. Epistaxis may give rise to error through swallowing of the blood and subsequent vomiting. For this reason it is always well to examine the nasal cavity carefully and to look for polypi and other source of nasal hemorrhage.

3. Having excluded other sources, one must decide *whether the hemorrhage be gastric, duodenal, or œsophageal.*

*Œsophageal Varices.*—There is nothing distinctive about the hemorrhages from the œsophagus. Œsophageal varices are most commonly associated with early cirrhosis of the liver, and one should therefore examine carefully for it. The evolution of the condition may help the diagnosis. In two-thirds of such œsophageal hemorrhages the patient improves, but recurrence takes place after intervals of days, months, or years. Sometimes they are fulminating in character. *Œsophageal cancer* may also simulate gastric ulcer, but has other evidences of malignant disease. *Œsophageal ulcer* causes pain after swallowing, increased secretion and regurgitation of mucus and food, and progressive signs of stricture.

*Duodenal hemorrhage* from ulcer is sometimes accompanied by hematemesis. Men are more commonly afflicted. As a rule, the stools show the first evidence of this condition. The pain is usually situated more to the right; it occurs later after meals than does that of ordinary gastric ulcer (two to four hours) or, at all events, is increased at that time; the digestive signs of pain, etc., coming on several hours after meals and the presence of HCl help to establish the diagnosis.

4. *The nature of the causative lesion* is often most difficult to determine, and is sometimes impossible. *Neuropathic hematemesis* is a problematical condition which is perhaps receiving less recognition each year; it is

presumably more common in nervous people, in females than in males; comes on after emotion with prodromata of heat, weight, or pain in the epigastrium and sometimes vertigo. It co-exists or alternates with hemorrhages from other organs which are presumed to have a similar cause. It is not usually fatal, and seems to have no effect upon the system in general. As a rule, patients thus afflicted pay but little heed to the hemorrhages when they occur. One should look for the other stigmata of hysteria. In all such cases, however, the exclusion of ulcer is not easy, and one will do well to diagnose the more serious anatomical lesion until further proof of a mere neuropathic origin is possible.

*Vicarious hemorrhages* usually occur in the absence of any gastric signs, have more or less periodicity, and at best are quite rare. They occur either at the time of the menses, or at times quite apart from that period. The menses may be absent and replaced by the hematemesis, the latter may coincide, with diminished menstrual flow. Legroux had a patient in whom monthly hematemesis occurred during the first seven months of pregnancy.

*Varices* in the stomach are very rare, and doubtless have the same causes as those in the œsophagus. Letulle found only two cases in sixteen years.

*Venous Stasis*.—Although varices are rare, dilatation of veins is common, and a rupture of the capillaries of the mucous membrane frequently occurs, as in cirrhosis of the liver, inflammation or tumors of the pancreas, cancer of the gall-bladder, wounds in the vicinity, etc. In the vomitus of peritonitis and intestinal obstruction there may be a little showing of blood; perhaps these types are infectious in nature.

*Hemorrhagic Erosions*.—These show only bleeding and few or no other symptoms. Often the blood is found only in the washings from the empty stomach and usually then associated with chronic gastritis. The use of the term to indicate a special disease as suggested by Einhorn is disputed by Elsner and others. The bleeding may occur by the mouth or the rectum, as in latent ulcers. Such cases are rarely fatal, and usually occur in men who are in poor condition, with advanced tuberculosis, or alcoholics with cirrhosis, etc. C. H. Miller attributes many gastric hemorrhages to erosions from swollen or ruptured lymphoid follicles in the stomach mucosa which has become thinned, while the basement membrane is unusually thickened. Thus the follicles are less covered, and under abnormal conditions, many lymphoid follicles become swollen, disintegrated, and softened. They in this way reach the surface, and may burst through the mucosa, thus leaving the basement membrane temporarily exposed to the gastric juice, which digests some of the numerous vessels of the submucosa. Hemorrhage then occurs.

*Miliary aneurisms* of the submucous arteries as a part of generalized aneurisms cannot be distinguished clinically.

*Simple Ulcer of the Stomach*.—Hematemesis coming on in healthy individuals or in those who have suffered from stomach disorders is due in the majority of cases to ulcer in some stage. The history with the symptom complex, the oft-recurring hemorrhage in youthful subjects with good appetites and good albumin digestion, the presence of HCl

in the contents, and the absence of cachexia aid in determining the presence of ulcer. The important point is not so much the exact diagnosis of the lesion, as the diagnosis of the value and possible success of intervention. The hemorrhage is often single and fulminating, as happens with the type of cases known as "exulceratio simplex." The term should become obsolete in the light of modern experience.

*Cancer* of the stomach is usually easy to diagnose from the history and the findings. The patient is older, with anemia, perhaps cachexia, anorexia, no HCl in the contents, but lactic acid instead, etc. While sometimes hemorrhage in cancer is acute and fatal, as a rule, bleeding is small, recurrent, and of a coffee-ground appearance. Occult blood in the stools is much more constant. However, many exceptions occur, and all possible factors must be considered together.

6. *Are the Ulcer and Vessel Accessible for Operation?*—Fresh ulcers usually erode the superficial vessels in the wall and are readily reached; old ulcers may be adherent to the pancreas and liver and are sometimes hollowed out. Adhesions form beyond the limits of the organ and are deeply situated, fixed in immobile tissues, perhaps hard or friable, the vessels are deeper, less accessible, and often larger. In a word, they erode rather the extrinsic arteries, such as the splenic, and make operation difficult, perhaps impossible.

**Prognosis.**—This depends chiefly upon the cause and, to a less degree, upon the severity of the hemorrhage. In serious general conditions hematemesis is one of the worst prognostic symptoms. When blood flows from outside structures into the stomach the prognosis is bad. In poisoning cases the amount of hemorrhage itself is of no prognostic importance unless the contents be putrid, in which case deep ulceration may be suspected and death may follow from sepsis or perforation. It is often difficult to differentiate between rupture of the small and the large vessels, and statistics vary very much because there is nothing in the evolution of the condition or in the antecedent hemorrhage which can prognosticate a recurrence or progressive gravity or origin; one cannot say from the amount of blood and the area of pain what vessel is affected or whether the hemorrhage will recur. The most copious hemorrhages may have no visible anatomical lesions of the mucosa. Large hemorrhages, however, are rarely fatal (3 to 4 per cent., Lebert).

Sometimes in gastric ulcer hemorrhage causes cessation of all the other signs; in cirrhosis of the liver that organ diminishes in size after a hematemesis. The cause is often more serious than the hemorrhage itself. In ulceration the prognosis is difficult to determine. Hyperacidity after the hemorrhage may act as an irritant and cause renewed ulceration and bleeding. For one month after a severe hemorrhage the condition continues serious, but from that time onward becomes less so, so far as life is concerned, but there is always the same uncertainty as regards recurrence. After eight to ten days the prognosis may be given as good, because of thrombus formation, although one must always keep in mind the possibility of hemorrhage from another part of the ulcer where a newly attacked vessel has opened. In cancer, hematemesis may usually be considered as a fatal sign because indicating advanced disease, although exceptions occur with bleeding at an early stage.



Preble concludes, from an analysis of 60 fatal cases of hematemesis with subsequent autopsies, that: (1) While not rare, fatal hemorrhage is at all events not common in cirrhosis of the liver. (2) The first hemorrhage in cirrhosis is fatal in only one-third of all cases. (3) Œsophageal varices are the source of the bleeding in 80 per cent. of cases; in half of these, ruptures were found and are probably much more common than is generally realized. (4) Fatal hemorrhages sometimes occur from invisible ruptures of numerous capillaries of the gastric mucous membrane, and, as a rule, there are some accompanying signs of early cirrhosis of the liver.

**Treatment.**—The indications are as follows: (1) Prophylaxis, when the possibilities of hematemesis are recognized. (2) Discovery of the etiological factor. (3) Control of the hemorrhage as quickly as possible. (4) Prevention of its recurrence. (5) Prevention of injurious sequelæ.

*Prophylaxis* depends upon the discovery of the possible underlying condition and its judicious treatment. Control of the hemorrhage requires *rest* in general and of the stomach in particular. The patient should be put to bed with the head low and kept as quiet as possible. All tight clothing should be removed and the patient encouraged with the explanation that hematemesis of itself is of no very serious import. Should faintness supervene, the face should be sprinkled with cold water, ammonia placed beneath the nostrils and if necessary camphor oil, ether, or caffeine, given hypodermically; a hot bottle may be placed to the feet. In the most serious cases an intravenous saline injection may be given and the arms and legs bandaged. An ice-bag may be suspended from a cradle so that it will come into gentle contact with the epigastrium. All food should be stopped for three days and the patient should be allowed only some ice to suck, but not to swallow. After three days, nutrient enemata may be given, three times daily. No food should be given by mouth until after the first week, and then, only gradually, boiled milk, broth, or gruel.

Lavage of the stomach is best avoided, so, too, all local hemostatics. General hemastatics are perhaps beneficial; adrenalin, in doses of 25 drops of the 1 to 1000 solution by mouth daily has apparently been of service. One may use rectal injections of calcium chloride, 4 to 8 gm. (3j to ʒij) daily or gelatin is sometimes useful by the mouth. The reflex effect of heat as administered by hot rectal injections (115°) has been much recommended.

**Accessory Treatment.**—Cold water enemata are useful for retained blood in the bowel. For the anemia, which may persist, one should give good food, and iron if the patient bears it well.

**Surgical Interference.**—*Indications.*—The blood count and estimation of hemoglobin *per se* are of little value. Appreciation of the general condition is more important than an estimate of the hematological state. If a low blood count has supervened on a previous chlorosis the condition is more grave. The pulse has doubtful value. The amount of hemorrhage is also of little importance as compared with its recurrence, which implies an end to medical treatment. For general surgical indications see the section on the Treatment of Gastric Ulcer.

## CHAPTER VI

### DISEASES OF THE INTESTINES

BY ALFRED STENGEL, M.D.

#### PHYSIOLOGY OF THE INTESTINAL TRACT

UNFORTUNATELY our knowledge of the physiology of the intestines has not yet proved of much practical value in the study of intestinal diseases or their treatment. The newer physiology of digestion (both gastric and intestinal) gives promise, however, of some practical applicability in the near future, and for this reason requires to be kept prominently in mind.

**Motor Function of the Intestines.**—The movements of the intestines serve three important purposes: (1) The onward movement of the contents; (2) thorough mixture of the chyme with the digestive secretion and close contact of the contents with the absorptive mucous membrane; (3) the propulsion of the venous blood and chyle away from the bowel. The old idea that the purpose of intestinal movements is to cause the passage of the intestinal contents toward the rectum has been disproved by recent investigations, which show that certain conspicuous movements of the bowel serve the purpose of thoroughly churning the contents and thus mixing the chyme and the digestive fluids and at the same time bringing the contents of the bowel into more complete contact with the mucous membrane.

Three forms of movement are recognized: (1) Peristalsis proper; (2) rhythmic segmentation; (3) antiperistalsis.

**Peristalsis Proper.**—Peristalsis proper, or the movement that causes the forward flow of the bowel contents, is a wave-like contraction that runs for some distance, gradually diminishing toward the end of its course, where a new wave starts up. The bowel contracts behind the contents and relaxes in front of them (Starling). These movements vary in rapidity and strength normally, and may become excessive in pathological states. Violent stimulation may cause a tonic contraction of a segment or a considerable portion of the bowel. The peristalsis of the colon causes an alternate protrusion and retraction of the haustra.

**Rhythmic Segmentation.**—In skiagraphic studies of the movements of the intestinal contents Cannon found that constrictions occur at various places, and the portions of the bowel between the constrictions may subdivide by secondary segmentation. The segments subsequently reunite and divide with renewed contractions. As many as thirty segmentations a minute were observed. These segmentations involve the contents of the bowel and do not indicate the kind of contractions

that occur in the wall between the segments. Possibly the swaying movements or waving movements described by Raiser may be the occasion of the segmentation. These are backward and forward contractions and relaxations affecting a limited part of the bowel and running in a direction parallel to its length. There is no appreciable narrowing of the lumen of the bowel. Such contractions might very readily divide the contents of the bowel into segments. Rhythmic segmentation continues during sleep, but may be inhibited by excitement. These movements cause a churning of the contents of the bowel and perhaps to some extent aid peristalsis proper in their onward movement.

**Antiperistalsis.**—Cannon has found this to be the important motor phenomenon of the large intestine. When the contents of the ileum are emptied into the large intestine they are carried forward for some distance. Antiperistaltic waves then begin and run to the ileocecal valve. A new significance is thus made manifest for the valve. The antiperistaltic waves working toward the closed valve churn the fluid contents and promote absorption. From time to time proper peristaltic contractions move the contents farther toward the rectum.

**Mechanism of the Movements.**—The movements of the bowel are caused by the irritating effect of their contents: solid, liquid, or gaseous. When empty, the intestines always are quiet. The irritation of the contents may be mechanical or chemical. Indifferent substances may act by their temperature or mere bulk. Of gases, hydrogen, oxygen, and nitrogen are indifferent, while carbon dioxide, sulphuretted hydrogen, and the hydrocarbons stimulate peristalsis.

Englemann believes the stimulus is transmitted through the bowel from muscle cell to muscle cell, but Nothnagel insists that nervous influences are always necessary, as do Gad and Luderitz. The stimulus to peristalsis originates in the plexus of Auerbach. The plexus of Meissner is concerned with the contractions of the muscularis mucosæ. Bayliss and Starling believe the swaying movements are myogenic in origin.

**External Nervous Mechanism.**—Stimuli are carried to the intestine through the vagus, and irritation of this nerve causes movements of the whole small intestine and upper half of the large. Irritation of the splanchnic nerves inhibits movements. Cannon, however, has found that section of the splanchnics or of the vagi and splanchnics disturbed normal peristalsis very little. Other observers, like Bach and Ehrmann, found that the splanchnic nerve is the motor nerve of the longitudinal fibres and the inhibitory nerve of the circular fibres, while the vagus stimulates the circular and inhibits the longitudinal. Bayliss and Starling deny any motor functions to the splanchnic. The lower half of the colon and rectum are innervated through the inferior mesenteric plexus and hypogastric plexus.

**Pathological Peristalsis.**—Various modifications of peristalsis may be met with. These may consist simply of excessive contractions, but in some cases rolling movements (Nothnagel) cause a contracted loop of the bowel to rotate like a wheel and then relax, while in other cases tonic contractions of a segment of bowel cause a stiffening and narrowing of this portion, which may last some time before it slowly relaxes.



*Varieties of Pathological Peristaltic Movements.*—(1) Increased peristalsis, (2) tonic contractions; (3) antiperistalsis.

*Increased peristalsis* may occur: (1) When the bowel contents are abnormal; (2) after the administration of purgatives; (3) after thermic or chemical irritation; (4) after emotional shock; (5) in neurasthenia; (6) from inflammations; (7) in cases of stricture of the bowel.

*Tonic Contractions.*—When the intestine is empty these convert the tube into a solid cord of a pale color. When a large part of the bowel is affected the abdomen may be scaphoid, as in certain cases of lead colic. Tonic contractions of a loop filled with contents may cause pain. Ordinary and even excessive peristalsis alone does not produce pain.

*Pathological antiperistaltic movements* are found only in the large intestine, according to Nothnagel. Others, however, believe that such waves may affect the small intestine as well. Greutzer showed that fluid containing free particles introduced into the lower bowel may find its way high up, even to the stomach, in a few hours. This upward movement seemed to occur most actively when the fluid was a sodium chloride solution. It did not occur with potassium chloride or hydrochloric acid solutions. Nothnagel has shown that sodium chloride applied to the external wall of the bowel causes upward movements running over several centimeters.

**Chemical Processes Occurring in the Intestine.**—The digestive processes that take place in the intestinal tract are effected by secretions from the glands and lining cells of the intestinal mucous membrane itself; but, to a still greater extent, by secretions poured into the intestine from the liver and the pancreas. The important secretions are: (1) The pancreatic juice; (2) the bile; (3) the intestinal secretion.

**The Pancreatic Juice.**—This alkaline liquid is a thin and somewhat watery fluid having a specific gravity of about 1007.5. The amount varies greatly, and cannot be stated with any certainty. In one case in which a permanent fistula existed (Glaessner) the amount was from 500 to 800 cc. per diem; but there is reason to believe that the fluid may not have been a pure pancreatic secretion. The secretion of pancreatic juice begins soon after food has been taken into the stomach, and reaches its maximum during the second to the fourth hour after that time. The character of the food influences, to some extent, the amount of secretion and the time of its maximum flow; and the rate of secretion seems to be especially dependent upon the promptness with which ingested food is discharged from the stomach into the duodenum.

The mechanism of pancreatic secretion has been determined by physiologists. It was first shown by Dolinsky, in 1895, that acids brought into contact with the mucous membrane of the duodenum promptly excite pancreatic secretion. This effect of the acid is certainly to a large extent independent of any influence upon nervous mechanisms, since the result occurs after section of the vagus and splanchnic nerves, quite as readily as when these nerves are intact. Bayliss and Starling have demonstrated the probable mode of action. They found in the mucous membrane of the duodenum an enzyme, *prosecretin*, which, under the influence of a 0.4 per cent. solution of hydrochloric acid, is

converted into *secretin*. The latter is absorbed and, reaching the pancreas through the blood, stimulates it to activity. It is not improbable that the HCl of the gastric contents may also exercise some effect upon the secretory and nervous mechanisms of the intestinal mucous membrane, but this is not of considerable importance. That secretin is carried to the pancreas in the blood has been proved by the fact that the pancreas may be stimulated by hypodermic injection of secretin.

The ferments of the pancreatic juice are: (1) The proteolytic ferment, trypsin; (2) a diastasic ferment, amyllopsin; (3) a lipolytic ferment, lipase or steapsin.

*Trypsin*.—It has been claimed by some that this is not a single body, but that a variety of trypsins, of different stability, occur. It has also been shown recently that trypsin is secreted in the form of a pro-enzyme, trypsinogen, which is inoperative as a proteolytic ferment until activated or converted into trypsin by an enzyme derived from the duodenal mucous membrane known as enterokinase. Bayliss and Starling claim that the trypsinogen cannot be converted into trypsin except through the action of this duodenal ferment.

Trypsin acts upon proteins in alkaline, slightly acid, or neutral media. Albumins are dissolved by its action without swelling, and, except serum albumin, are converted first into a globulin insoluble in water; later, into peptones soluble in water. Trypsin probably, however, carries the hydrolysis of certain peptones still farther, producing leucin, tyrosin, and other simple bodies. According to some recent observations, the prolonged action of trypsin destroys all peptones, leaving only end-products of a simpler nature.

*Amylopsin*.—This enzyme is similar to, if not identical with, the ptyalin of the saliva. It hydrolyzes starches, with the formation of maltose and achroödextrin. These substances are further acted upon by the maltase of the intestinal secretion, and converted by this into dextrose. According to Hoffmeister, the maximum amylolytic effect occurs in the presence of a moderate acidity.

*Lipase or Steapsin*.—This ferment was discovered by Bernard in 1849. It has never been isolated. Lipase splits neutral fats, with the formation of fatty acids and glycerin. The fatty acids thus liberated unite with alkalis to form soaps, the latter being further utilized for the emulsification of other fats. The recent experiments of Kastle and Loewenhardt indicate that, by reversed action, lipase causes a synthesis of the products of the splitting of fat, with the re-formation of the original fat. This synthetic action is believed to take place in the intestinal wall, as well as in the tissues. Lipase is a widely distributed enzyme, being found in the blood and in many tissues.

**Bile**.—The quantity of bile varies considerably under different conditions. The maximum secretion occurs about an hour after a meal. Protein foods increase the amount of secretion; fats reduce it; carbohydrates appear to have little effect. Starling believes that the secretion of bile is initiated by the action of a hormone (analogous with secretin) formed by the action of the acid gastric contents on the mucous membrane in the intestines. The total quantity of bile in twenty-four hours

varies from 500 to 600 cc. (Ranke, Wittich). Hammarsten found similar figures in his observations of seven cases of biliary fistula in man. The bile is a clear, alkaline, mucoid liquid, of yellowish to brownish color. Its important constituents are bile-acid salts (glycocholates and taurocholates) and pigments (bilirubin, biliverdin, etc.). The mucoid character is due to the presence of a nucleo-albumin or true mucin. Various other less important substances are present. There are also ferments, diastasic and lipolytic, which supplement the action of the pancreatic secretion.

The principal action of the bile in digestion and food absorption is its relation to the emulsification of fats. The alkalis contained in the bile unite with the fatty acids to form soaps, and the bile directly aids in the splitting of the fats. It has been held that the bile exercises some antiseptic effect on the intestinal tract; and it probably has some influence in stimulating intestinal peristalsis.

**Succus Entericus.**—The secretion of the intestinal mucous membrane is the product of various tubular glands of the small intestine. The quantity of the secretion has been estimated by Prigl as being as much as three liters a day. It is probable, however, that the amount varies greatly in different cases and under different conditions. Investigations have shown in the intestinal secretion and in the mucosa of the small intestines a number of important enzymes, of which the following have been most thoroughly worked out: enterokinase, crepsin, inverting enzymes, and secretin.

*Enterokinase.*—This has been found in the mucosa of the duodenum, and seems to be the ferment that actuates trypsinogen, converting it into trypsin.

*Secretin* is a stable body existing as a prosecretin in the intestinal mucous membrane. Under the influence of the acids of the gastric contents the latter is converted into secretin, which is absorbed, and reaches the pancreas through the circulation, stimulating this organ to activity.

*Erepsin* completes the hydrolysis of proteins, acting upon the deutero-albumoses and peptones prepared by the preliminary stages of digestion.

*Inverting enzymes* convert disaccharids into monosaccharids.

Besides these substances, a secretin has been thought to exist which originates in the intestinal mucous membrane and, after absorption, stimulates the liver to activity.

## ABSORPTION OF FOODS IN THE INTESTINE

The products of digestion are mainly absorbed by the bloodvessels, and, entering the portal system, are carried to the liver. Fats, however, after their cleavage in the intestines, are resynthesized in the intestinal mucous membrane and absorbed through the lacteals. *Carbohydrates* are absorbed as simple sugars, monosaccharids, the disaccharids being converted into the simpler form by the action of inverting enzymes in the small intestine. When an excess of sugar is administered there may be direct absorption without such preliminary change. *Fats* are in part split into their constituents, fatty acids and glycerin, and in part



emulsified, after which absorption through the mucous membrane occurs. The cleavage products are synthesized and, with the emulsified fat, enter the lacteals. Proteins are absorbed after digestion by pepsin, trypsin, and erepsin; and are absorbed as peptones or proteoses. To some extent, however, simpler bodies, such as leucin, tyrosin, arginin, etc., may be formed, and may be later synthesized to reconstruct the albumin of the tissues. It has been claimed that proteins may be absorbed without preliminary digestive alteration.

To some extent, products of digestion that have escaped absorption in the small bowel are absorbed in the large intestine. Under normal conditions the main absorption that occurs in this part of the intestinal tract is that of water; and, as a consequence, the fluid contents of the upper part of the large intestine become more and more concentrated and finally solidified as they approach the rectum.

### THE INTESTINES AS EXCRETORY ORGANS

The importance of the intestines as excretory organs is not perhaps as yet fully recognized. It is well known that in certain diseases large quantities of serum may be poured into the bowel, carrying toxic matters of various sorts, chemical, bacterial, etc. Certain inflammatory, ulcerative, and necrotic processes in the mucosa doubtless result from such excretions. Investigations with certain drugs and chemical bodies of other sorts have given direct proof of this excretory function of the intestines. Among other substances, iron, calcium, strontium, lithium, and cesium have been found to be largely excreted through this channel.

### AUTOMATIC MECHANISM IN INTESTINAL PROCESSES

The entrance of chyme into the bowel and the secretion of various digestive fluids is regulated in an automatic manner. When the gastric contents reach a certain degree of acidity from the presence of free hydrochloric acid a stimulus is exercised which occasions the opening of the pylorus and the expulsion of the acid chyme. This next acts upon the intestinal mucous membrane, and occasions a stimulus which effects the closing of the pylorus. At the same time, the acid acting upon the mucosa of the duodenum liberates secretin and possibly a hormone which stimulates the liver. To a minor degree, perhaps, the acid excites nervous stimuli, which aid in promoting pancreatic and hepatic activity. The alkaline bile and pancreatic juice entering the duodenum reduce the acidity of the chyme, neutralize it, and render it alkaline, thus establishing conditions favorable for the action of the various ferments. When the acidity of the duodenal contents has been neutralized, the stimulus which caused the closing of the pylorus is removed and a reopening of the pylorus with discharge of more chyme follows.

The inert tripsinogen of the pancreatic juice is converted into trypsin by the ferment enterokinase, which like secretion is liberated from the

intestinal mucosa under the influence of the acid chyme. The other ferments derived from the intestinal mucosa are quite possibly secreted as a result of the same cause.

### THE FECES

The feces consist of undigested and indigestible residues of food, together with altered digestive secretions, certain excretions from the intestinal mucosa, and a notable percentage of bacteria. According to the investigations of Strasburger and others, not less than a third of the dried substance of the feces consists of bacteria, and in some pathological conditions the amount is even greater than this.

The quantity of fecal matter depends upon a variety of conditions. The amount of food, its digestibility, the absorptive power of the intestines, the quantity of bile or pancreatic juice, or of mucus thrown off by the intestinal glands, and the activity of bacterial processes in the bowel all influence the amount. Age, occupation, or habits of life, and functional conditions or diseases influencing the degree of peristalsis also exercise a decided influence. On a mixed diet, 120 to 150 grams, representing from 30 to 37 grams of solid residue, are passed in twenty-four hours. The greater the quantity of indigestible residue, the larger the fecal output. The variation of amount in different individuals is very considerable, as is shown in a table of Harley and Goodbody,<sup>1</sup> who found among 188 cases variations from 30 to 282 grams with a mixed diet. The average was 102.8 grams.

The *color* of the feces is largely dependent on the character of the food. With a mixed diet the color is a light or dark brown, and is largely due to urobilin. Large amounts of meat cause a darker color of the stools, on account of the presence of altered blood pigment, hematin, and sulphide of iron. The greenish color seen when an abundance of green vegetables is eaten is due to chlorophyl. The feces passed by persons whose diet consists largely of milk are light yellow, the light color being caused by the quantity of fat in the excreta. Bright-green stools in children or adults may be due to bacterial pigments or to the passage of unaltered bile. Sometimes there is a light color resulting from the presence of bubbles of gas mixed with the fecal matter. The light color of feces in certain liver diseases is due to absence of bile and its derivatives. (See *Acholic Stools*.) Some medicines, especially iron, bismuth, lead, and silver, cause black stools; while others, like senna, rhubarb, and hematoxylin, cause a yellowish or reddish color.

The *odor* is due to skatol and volatile fatty acids. In fermentative and putrefactive conditions various aromatic bodies may impart a sour to putrid odor. Sometimes all trace of odor is wanting.

The *consistency* is normally dependent upon the amount of water, fat, and mucus associated with the insoluble residues. Lack of digestion and absorption of fat or excess of fat in the diet, excessive water drinking,

<sup>1</sup> *The Chemical Investigation of Gastric and Intestinal Diseases*, 1906.

abnormal excretion of mucus from the intestinal mucosa, and increased peristalsis which hurries the contents of the bowels through the large intestine, all tend to make the stools soft, semiliquid, or even watery. In certain pathological conditions (choleraic diarrhœas) there is an abundant watery outpouring into the bowel, and large watery evacuations are the result. The stools are more firm than normal when the food contains but little indigestible residue or when in the various forms of constipation the contents are retained too long in the large intestine.

The *reaction* of the normal stool is usually alkaline or neutral. Sometimes, however, a faint acid reaction is met with. Diet and pathological conditions of the bowel may occasion more decided acidity.

The *chemical composition* of the feces varies widely. The amount of water in the feces of persons on a milk diet was found to vary from 73.29 to 79.32 per cent., and in persons on a mixed diet was on the average 75.72 per cent. (Harley and Goodbody). Of the organic substances met with normally, fats and their derivatives, soaps, albumin, mucin, phenol, indol, skatol, fatty acids and their salts are important. The daily excretion of nitrogen in fasting persons has been found to vary from 0.17 gram to 0.446 gram per day, the average being 0.254 gram (Schmidt and Strasburger). With a mixed diet Harley and Goodbody found a discharge of from 0.30 to 1.55 grams per day, the average being 0.97 gram. Excess of diet, especially such as contains a large amount of residue, causes progressive increase in elimination of nitrogen. The percentage absorption of nitrogen of the food, with various forms of diet, varies from 90 to 96 per cent. Approximately, one-half of the nitrogen of the feces is contained in the bodies of the bacteria. Fat, like nitrogenous substances, is excreted in the feces even when the patient is fasting. The total excretion per day under these circumstances is from 0.57 to 1.21 grams (Schmidt and Strasburger). With ordinary diet, either milk or mixed, the daily excretion is from 3 to 7 grams, the proportion of absorption varying from 91 to 98 per cent. The character of the fats ingested, and especially the melting point, determines to some extent the degree of absorbability. Phenol, skatol, and indol are products of bacterial processes, and their amount is to a large degree dependent on the activity of such processes.

Among the *inorganic* constituents are chlorides and carbonates of alkalis, phosphates of the alkaline earths, and other inorganic salts in small amounts. The amount and source of the calcium salts have excited special interest. It is generally believed that calcium is to an extent eliminated by the large intestine, although some deny this.

*Microscopic* examination serves to discover undigested particles of food, such as meat fibres, connective tissue, and starch bodies, that may be significant of different forms of intestinal or gastric disease. In inflammatory conditions mucus, pus cells, epithelium, and blood corpuscles may be found, and occasionally portions of exfoliated mucous membrane or portions of tumors of the bowel may be recognized.

*Mucus* may be found as gelatinous or shred-like particles or as considerable masses, visible to the naked eye, or as stringy formations visible under low powers of the microscope. Mucus from the upper



bowel is often colored yellow by bile pigments; that from the colon or rectum is grayish or white. Certain small masses of gelatinous material that resemble mucus on superficial examination, presenting a yellowish color, may prove to be albuminous substances, and small globular masses, like frog spawn, are found to be derivatives of vegetable matter of the diet. Among the crystals found in normal feces triple phosphates are the most common. Crystals of neutral phosphate of lime, and of oxalate of lime, cholesterolin and Charcot-Leyden crystals, may also be found.

**Acholic, Colorless, and Fatty Stools.**—*Acholic stools* are yellowish gray or actually white in color. To a large extent this is due to the absence of hydrobilirubin, the normal pigment which is a derivative of bile pigment. In any condition in which complete obstruction of the hepatic or common bile duct occurs the feces become of the color described. Sometimes the same stool occurs without jaundice and without obstruction of the bile duct. In these cases the light color is usually due to the presence of enormous quantities of fat which may be dependent upon disease of the pancreas, obstruction of the pancreatic duct, or to various diseases of the intestines which interfere with the absorption of fat. Chemical analyses have shown in these cases that urobilin is present, although its color is obscured by the excess of fat. Another explanation of colorless stools in the absence of diminished outflow of bile is that the bile pigments are converted into colorless substances (leuko-urobilin). In these cases the stools give reactions for bile, and may be devoid of an excess of fat.

*Colorless stools* may occur independently of any disease of the liver or pancreas. In various forms of intense diarrhœa, as in dysentery, or certain cases of enteritis, in tuberculous peritonitis in children (Berggrün and Katz), and occasionally in various other diseases, the feces may be quite colorless. A diminished excretion of bile may play some part in these conditions, but in most cases the altered color is the result of the amount of unabsorbed fat.

*Fatty Stools.*—From what has just been said it will be seen that various conditions may occasion excess of fat in the stools. As a rule, however, the term fatty stools is applied to cases in which masses of fat can be seen in the feces or in which there is a distinctly oily appearance of the excreta. When somewhat watery, oil may collect on the surface of the liquid. Microscopically, fat crystals in large numbers are discovered. Fatty stools may result from:

1. Increased ingestion of fat, as in persons consuming large quantities of milk, cream, olive or cod-liver oil.

2. When absorption of fat is interfered with (*a*) by diseases of the bowel, such as enteritis, ulceration, etc., or (*b*) by active peristalsis and the prompt evacuation of the upper bowel.

3. When bile is excluded from the bowel by obstructions of the bile duct. The excess of fat associated with acholic stools has been mentioned.

4. When disease of the pancreas or obstruction of its ducts causes deficiency of pancreatic juice. In these conditions the most typical fatty stools are met with. A veritable fatty diarrhœa may occur. The association of obstructive biliary conditions often aids in the production

of the fatty stools of pancreatic disease. A difference between the fatty stools of biliary obstruction and of lack of pancreatic secretion has been indicated by Müller. In the former condition a large percentage of the fat present (84.3 per cent.) had suffered cleavage, whereas in cases of lack of pancreatic fluid only 39.8 per cent. had been converted.

**Intestinal Sand.**—Occasionally gritty, sand-like material is discharged from the intestines. This usually consists of granular particles of grayish or reddish color, and on chemical examination has been found to contain various organic and inorganic substances. Duckworth and Garrod found, in a case in which chemical analyses were made, the following constituents: water, 12.40; organic matter, 26.29; inorganic matter, 61.31. The inorganic constituents consisted of calcium oxide, 54.98; phosphorus pentoxide, 42.35; carbon dioxide, 2.20; residue, containing traces of magnesium and iron, 0.47. Analyses by other investigators have given similar results (Harley and Goodbody). The term intestinal lithiasis has been applied to this condition, in the thought that there is a particular form of catarrh of the intestines with the discharge of calcareous matter comparable to the formation of calculi elsewhere.

Intestinal sand is probably formed in the colon, as it usually contains considerable urobilin and little bile-pigment. It must, therefore, be produced in a part of the intestines in which the conversion of bile-pigment has progressed considerably. The condition with which intestinal lithiasis is most commonly associated is mucous colitis.

A condition (false intestinal sand) that requires differentiation is that in which various residues of vegetable food are passed. These may have a sandy character that suggests true intestinal sand.

### BACTERIOLOGY OF THE INTESTINAL TRACT

Enormous numbers of bacteria normally occupy the intestinal tract. A conception of the number may be gained from the knowledge that Strasburger found that one-third of the weight of the dry residue of the feces consists of the bacterial bodies. In normal adults the weight of the dried bacteria passed in twenty-four hours is as much as 8 grams; while in certain dyspeptic conditions it may reach 14 to 20 grams. When habitual constipation is present the weight falls to 5.5 or as low as 2.6 grams.

**Distribution of Bacteria in the Intestines.**—Billroth recognized that there are far more bacteria in the large than in the small bowel. Systemic examinations show a progressive increase in number from the duodenum to the large intestine. The duodenum and jejunum may be entirely free six hours after meals (Cushing and Livingood). Below the jejunum bacteria are probably never absent after birth.

The kinds of bacteria as well as the number vary in different parts of the digestive tract. This is doubtless due to changes in the conditions in different situations. The gastric secretion, the bile, and the pancreatic juice have probably only a moderate effect in destroying bacteria ingested with food. Smith and Tennant claimed that the secretions of the intestinal mucosa have an inhibitory effect on the multiplication of bacteria. The condition of the intestinal contents with reference

to the process of digestion and the presence or absence of oxygen are factors that have an influence on the number and kind of organisms present in different localities. Herter showed that the conditions are practically anaërobic below the middle of the small intestine.

The organisms generally found in the duodenum and jejunum are various forms of micrococci and other varieties swallowed with food or saliva. In the lower part of the small intestine are found the obligate intestinal bacteria which belong respectively to the groups *Bacillus lactis aërogenes*, *B. coli*, and *B. bifidus communis*. These forms remain as permanent inhabitants and are not dependent on ingestion with food. Although capable of exercising pathogenic properties under certain circumstances, they are ordinarily so adapted to the organism, and it to them, that their presence is devoid of any pathological effects. An evidence of their adaptation to the organism is seen in the fact that the serum of normal individuals has little agglutinative influence on these organisms. Although within the intestinal tract, they are practically outside the body, and whatever products are elaborated by their growth apparently have little effect on the system. The most abundant of the three forms of microorganisms named is the colon group. Cushing and Livingood found the maximum just above the ileocecal valve. Their number decreased decidedly in the colon.

Among the forms met with in the lower small intestine and in the large bowel are certain anaërobes, notably *B. putrificus* and *B. aërogenes capsulatus*. Recently considerable attention has been given to the possible pathological results of the growth of such forms (Metchnikoff, Herter). Many other microorganisms have been found in the intestinal tract under seemingly normal conditions.

The meconium before birth is sterile. Very soon after birth microorganisms are swallowed or enter the anus, and a considerable flora is soon present. In nurslings the *Bacillus bifidus* is the most abundant form in the large intestine, the *Bacillus coli* being less numerous. In bottle-fed children the dominant form, as in adults, is *B. coli* (Herter).

**The Significance of Bacteria in the Intestinal Tract.**—Are bacteria in the intestines to be regarded as a normal condition and necessary to life? Nuttall and Thierfelder kept young guinea-pigs, that had been removed from the maternal uterus by Cæsarean section under aseptic precautions, for some weeks in a sterile condition by feeding sterile food and allowing only sterile air to reach them. The animals gained weight and in every way developed as well as the controls. However, conclusions the reverse of those of Nuttall and Thierfelder have been arrived at by some other investigators, who found that animals did not develop in a normal manner when kept free of bacteria (Schottelius, Madame Metchnikoff, Moro). Pasteur and Nothnagel believed that bacteria are essential to physiological life, and certainly, whether essential or not, they are universally present and exercise a distinct effect on the intra-intestinal processes. The rôle of bacteria in the conversion of bile pigments into urobilin, the final decomposition of products of protein digestion by bacteria, the possible presence of enterokinase of bacterial origin (Dellezenne, Breton), and other evidences may be recalled.



Under ordinary conditions the bacteria of the feces are practically all dead. Klein estimated that a little over 1 per cent. are living forms, and Strasburger found even a lower proportion. The causes of this practical sterilization of the feces have not yet been determined with certainty. Possibly the changing reactions and other conditions at the different levels of the bowel may play some part, as may also influences exerted by the bowel wall and its secretions. Perhaps products of the bacteria themselves occasion their own destruction.

There is considerable evidence to prove that the normal intestinal flora is useful in protecting the individual against accidental pathogenic invaders. There seems to be little doubt that *B. coli* and *B. bifidus* exercise some inhibitory action on the growth of pathogenic organisms such as the putrefactive anærobes and various specific pathogenic forms. Conradi and Kurpjuweit attribute this effect to antibacterial substances elaborated by the *B. coli*. They believe, also, that the same substances destroy the organism itself, thus accounting for the nearly sterile condition of the feces. Lactic acid formed in the intestinal tract or swallowed with food may exercise a restraining influence on the growth of pathogenic (putrefactive) organisms. This may explain the controlling influence of a milk diet observed clinically in cases of intestinal putrefaction.

**Growth and Virulence of Intestinal Bacteria.**—Various digestive disturbances may increase the growth of bacteria by causing large amounts of nutritious material to pass down to the lower bowel. In habitual constipation, when practically all absorbable material is taken up in the small intestine, the number of bacteria in the feces is the lowest met with under any conditions. The total bacterial output was found to be as low as 2.6 grams as against as much as 20 grams in dyspeptic conditions and 8 grams in normal persons (Strasburger). Excessive feeding acts in the same manner as digestive disturbances, and in part as a result of the dyspeptic conditions caused by it. Catarrhal conditions of the bowel, the result of excessive multiplication of the bacteria or occurring independently, favor further increase of bacterial growth and increased virulence of the organisms. When ulcerations, erosions, or other lesions of the mucous membrane are present, the ordinarily harmless intestinal bacteria may gain access to the tissues and may occasion local or general infections. Sometimes a symbiotic relationship is established between different bacterial forms or between bacteria and protozoa. The *Bacillus coli*, for example, is said to grow in virulence in the presence of staphylococci and streptococci (Coco).

**Diagnosis of the Types of Intestinal Bacteria.**—Systematic culture methods are of course required to determine accurately the kinds of organisms present in the intestinal tract. Such examinations are essential in the diagnosis of certain specific disease such as cholera and dysentery; and occasionally in typhoid, paratyphoid, and allied infections. In other intestinal disorders simpler methods may serve to identify the prevailing types of invading organisms. Strassburger's method is as follows: Mix a portion of the feces with water and centrifugate; dilute the turbid supernatant water with two parts of alcohol; centrifugate and spread the sediment on glass slides; Gram-stain and counter-stain with fuchsin.

In such preparations the stools of breast-fed infants show a predominance of Gram-positive bacilli, while in bottle-fed children the Gram-negative *Bacillus coli* is conspicuous. In adults the latter type is especially marked, while a diet of milk and carbohydrates occasions the appearance of a small proportion of large-sized Gram-positive bacilli and one of meat in considerable amount that of Gram-positive micrococci.

**Treatment of Bacterial Invasions of the Intestinal Tract.**—The problem of disinfecting the gastro-intestinal tract has occasioned much discussion, but still remains unsolved. The most important element in treatment is the proper regulation of diet and the avoidance of all infection of food. This involves the avoidance of all putrefactive contamination of food by proper care in its preservation and preparation, and the withdrawal of such articles as cheese, uncooked fruit, or milk. The careful cleansing of the mouth is also an important element.

The quantity of food is of importance. Excessive eating occasions the passage through the intestinal tract of increased quantities of unabsorbed material and favors bacterial multiplication. A strict regulation and limitation of the diet is, therefore, desirable; and remedies such as hydrochloric acid, pepsin, pancreatin, and the like, which aid digestion, may prove beneficial. Sometimes an exclusive milk diet is useful, particularly when albuminous decomposition or putrefaction is conspicuous. In other cases, a strict limitation of carbohydrate foods is required. No general rule can be laid down as individual cases vary widely.

Intestinal antiseptics of various sorts have been tried; but so far none can be said to have a generally useful effect. Small doses of calomel may be helpful, and other laxatives or purgatives may be temporarily beneficial, by cleansing the intestinal tract. Betanaphthol, ichthyol, resorcin, salol, creosote, etc., have been tried, but appear to exercise little, if any, useful effect. Sometimes, as Steele showed, these remedies may cause more injury to the mucous membrane than to the bacteria; and may, therefore, increase rather than decrease the number of organisms and the activity of the putrefactive process. Sometimes astringent remedies, such as bismuth and tannin, may have a useful effect.

Renewed attention has been called to the possibility of influencing intestinal fermentation and putrefaction by the administration of cultures of bacteria. An old method was to administer brewer's yeast. More recently, Brudzinski, Metchnikoff, and Tissier have employed cultures of organisms that occasion lactic acid fermentation. The same principle applies to the administration of sour milk, buttermilk, koumyss, etc. The value of this form of treatment has not been determined. It is doubtful whether the extravagant claims will be substantiated.

### GASEOUS DISTENSION OF THE INTESTINES

The terms *meteorism* and *tympanites* have been applied to the occurrence of abnormal quantities of gases in the intestines, the former signifying acute, the latter chronic, distensions. Normally there is always a certain amount of gas in the bowels, consisting of the constituents of atmospheric air that has remained unabsorbed after having been

swallowed, and other gases derived from the blood or from fermentative processes in the intestines. Among the gases present are oxygen, hydrogen, ammonium, carbon dioxide, methane, and sulphuretted hydrogen. The oxygen is mainly that which gains access to the bowel from atmospheric air swallowed with food. It is, however, readily absorbed, and, consequently, disappears in the small bowel, the large intestine being practically free of it (Herter). Carbon dioxide is largely derived from the blood; and the other gases are mainly derivatives of fermentative processes. The amount of gas normally present is small, and is regulated by the absorptive processes and the discharge of any excess from the stomach or bowel. Abnormal accumulations may be due to increased swallowing of air, to active gas formation within the bowel, and to interference with absorption or escape of the gas from the intestines.

The formation of abnormal quantities of gas by fermentation is a frequent accompaniment of catarrhal conditions of the bowel and of functional intestinal indigestion. Various forms of fermentation may occur, such as those affecting principally carbohydrates; or others in which proteins or fats are involved. Sometimes such fermentative or putrefactive conditions are excited by indiscretions in diet, as when the patient eats excessively of readily fermentable food. With many individuals, milk is a common cause of the condition.

Gaseous distension due to failure of absorption or inadequate discharge of gas from the bowel is common in various intestinal diseases. Such distensions are habitually met with in cases of partial or complete intestinal obstruction. In these cases the interference with the discharge of gas from the bowel is the important factor. In catarrhal inflammation and intense congestion the accumulation of gas is due largely to the failure of absorption. This is strikingly illustrated in cases in which a portion of bowel strangulated by volvulus becomes enormously distended. The gases in such instances are partly due to fermentation within the loop, partly to the liberation of carbon dioxide from the blood and to the stagnation of the circulation preventing reabsorption.

In peritonitis and in certain conditions of nervous or functional weakness of the intestinal walls, gaseous distension results from the inability of the bowel to remove the accumulations.

In hysterical individuals, and sometimes in persons not manifestly hysterical, extreme distension of the abdomen or localized distension may occur. The name *phantom tumor* has been applied to this condition. In many cases it is paroxysmal and transient, but sometimes it proves quite lasting. Many of the instances, however, of supposed chronic phantom tumor have doubtless been cases of idiopathic dilatation of the colon. The explanation of phantom tumors has occasioned some difficulty. There is, probably in most cases, an actual increase in the amount of gas; but the distension is, in part, more apparent than real, being dependent to some extent upon contractions of the diaphragm and of the abdominal muscles. In other cases, a paresis of the abdominal muscles doubtless plays a part.

**Symptoms.**—The important symptom of meteorism, or tympanites, is the distension of the abdomen. This is usually uniform; but in some



cases it affects limited portions of the bowel, and therefore of the abdomen, more than others. Localized collections of gas are not infrequent in association with organic conditions of the bowel. The degree of distension may vary from slight fulness to enormous enlargement, the amount depending upon the resistance offered by the bowel itself and by the abdominal walls. Subjective symptoms are rarely wanting. In acute cases there is often marked discomfort or severe colicky pain. In the more chronic forms constant slight abdominal distress, accompanied from time to time by exacerbations of distension, is complained of. Loss of appetite, coated tongue, nausea, and a tendency to vomiting after slight indiscretion in diet, and other evidences of disordered digestion are frequent. General symptoms, such as drowsiness, listlessness, and a variety of nervous manifestations, including headaches, neuralgias, and even pronounced neurasthenic symptoms, are common.

On physical examination, the abdomen presents a certain type of elastic resistance that is usually quite characteristic; and on percussion the deep note of tympany is more or less pathognomonic. The liver and spleen may be displaced, and their normal areas of dulness obscured or almost obliterated. This is particularly important in the case of the liver, on account of the possibility of mistaking tympany for the accumulation of gas in the peritoneal cavity. In extreme cases the diaphragm is forced upward, and the heart may be displaced, sometimes to the extent of two or three intercostal spaces, and the bases of the lungs may be somewhat compressed. In these instances signs of pulmonary and circulatory embarrassment are usually present.

In cases of phantom tumor symptoms may be wanting, or the patient may complain of various subjective manifestations. A local gaseous distension may simulate an actual abdominal tumor. When the distension is extreme and the normal tympanitic note gives place to a duller tone on percussion, the simulation may be quite confusing.

**Diagnosis.**—The diagnosis of meteorism rarely occasions difficulty. The important question in the diagnosis is to determine the cause, and this requires a careful consideration of the many conditions in which such distension may occur.

**Treatment.**—In moderate cases due to irritative and fermentative conditions in the bowel, restriction and regulation of the diet may speedily relieve the condition. Remedies may, however, be required to reduce the distension more speedily. Various carminatives, such as oil of peppermint, menthol, chloroform, Hoffmann's anodyne, asa-fetida, and the like, are employed for this purpose.

Sometimes the use of laxatives or purgatives may be beneficial, but usually evacuation of the bowels is best accomplished by the employment of enemata containing asafetida or turpentine in saline solutions, soap-suds, etc. When the distension is excessive, a rectal tube may be useful in causing a rapid discharge of gas. The peristalsis may be stimulated by the use of eserine or pituitrin. Hypodermic injections of the sulphate of eserine, in doses of gr.  $\frac{1}{100}$  to  $\frac{1}{50}$ , repeated at intervals of three or four hours, sometimes act promptly and most satisfactorily.

Puncture of the distended bowel has been practised, but is a dangerous mode of treatment and cannot be advised.

## INTESTINAL INDIGESTION

This term is preferable to the name intestinal dyspepsia, sometimes applied to it, because the latter suggests the gastric digestion rather than that of the intestines. In a broad sense, *intestinal indigestion* may be used as a term denoting any form of interference with the normal intestinal functions, but it is more properly restricted to functional derangements, rather than to such as may attend organic disease. In inflammatory conditions of the intestines, in obstruction, in cases of ulceration, tumors, and the like, the normal digestive processes and absorption are interfered with; but these are promptly considered as direct consequences of organic troubles. Leaving such cases out of consideration, there remains a group of conditions in which, without gross organic disease, disturbance of the intestinal functions is met with.

**Etiology.**—Functional intestinal indigestion may be due to (1) lack of bile and pancreatic juice; (2) lack of secretion of the intestinal ferments proper; (3) bacterial fermentative processes.

Attention is directed to the effects of the withdrawal of biliary and pancreatic secretion in the discussion of fatty stools, acholic stools, and diarrhœa. Usually, in the consideration of intestinal indigestion, these conditions are not taken into account. Unfortunately, very little can be said regarding the functional results of insufficient secretion of intestinal ferments proper. That these secretions play an important rôle in the functions of the intestinal tract is entirely probable, in view of our present knowledge; but the clinical significance of derangement of these secretions has not been determined with any definiteness.

Disturbance of the intestinal digestion may be a secondary result of the disorders of gastric digestion. In cases of hyperacidity of the gastric contents the alkalinity of the bile and pancreatic juice may be insufficient to neutralize the acidity of the chyme, in consequence of which the reaction of the contents of the duodenum and jejunum remains acid, instead of being alkaline. This interferes with the normal pancreatic digestion, and at the same time subjects the mucosa of the upper small intestine to irritation. A similar effect may follow insufficient secretion of bile and pancreatic juice, in which case the normal acid chyme may fail of neutralization. Much more common is the development of acidity in the small intestine as the result of bacterial invasion. This is very common in infants and children. Bacterial decomposition of milk and other foods may occasion the formation of lactic, acetic, and other acids, and may thus interfere with pancreatic digestion and, at the same time, occasion irritations of the mucosa of the small bowel. The effects of these conditions are, first, an interference with normal intestinal digestion; second, an increased liability to bacterial activity; and, third, irritation of the mucosa.

**Symptoms.**—These are partly gastric and partly intestinal. Among the gastric manifestations, nausea, vomiting, flatulence, and sensory disturbances, such as heaviness or pain, may be mentioned. Among intestinal manifestations are gaseous distension and diarrhœa. The acid contents provoke an irritation of the upper bowel and the formation

of the excessive quantities of mucus. At the same time, peristalsis is increased by the irritation; and the semifluid contents of the upper bowel are hurried into the lower bowel and discharged before normal inspissation and chemical changes have time to occur. The stools are acid instead of alkaline, and frequently cause marked irritation of the rectum and anus. In children this becomes an important symptom; and intense irritation, sometimes extending to a considerable distance over the buttocks, may be met with. The movements are usually somewhat tenacious, on account of the admixture of excessive quantities of mucus, and commonly present a greenish color, on account of the presence of bacterial pigments or of unaltered bile. In a special form described by Schmidt, under the name of *intestinal fermentative dyspepsia*, the stools are of light color, foamy, and of a musty or sour odor, due to the presence of butyric acid. When functional indigestion persists, the irritation of the bowel readily passes into catarrhal inflammation.

**Diagnosis.**—This often presents great difficulty. In some instances the symptoms are vague and indistinct; and it may be difficult to determine that a continuous tendency to intestinal flatulence and slight disorder of the bowel is due to functional disturbance rather than to organic disease. In more acute cases, especially those occurring in children, the evidence is more trustworthy. The occurrence of mucous, gelatinous stools of green color, acid reaction, and sour or musty odor, is strongly significant of this form of disease. It is always difficult, however, to determine that an actual catarrhal enteritis has not supervened.

**Treatment.**—This requires close supervision of the diet. In the beginning of acute attacks, the withdrawal of all food may be advisable. In children, as well as in adults, the substitution of albumin water, broths, soups, or barley water for the ordinary diet, and especially for a milk diet, is advisable. Later, the food should be regulated according to the nature of the case. Sometimes, when fermentative processes and gas-formation are conspicuous, it is best to use only animal food, such as eggs, soups, jellies, and gelatin preparations; while in other cases, in which albumin decomposition predominates, gruels, cereals, and farinaceous foods generally, with smaller amounts of albuminous food, should be given.

The medical treatment is directed to the evacuation of the contents of the intestines and the removal of fermenting material. A full dose of castor oil, or repeated small doses, may accomplish this purpose. Calomel in small amounts (gr.  $\frac{1}{40}$  to gr.  $\frac{1}{10}$ ), two or three times daily, may exercise an antiseptic effect, as well as a slightly laxative influence. Other remedies like salol, betanaphthol, guaiacol carbonate, and ichthyol may be useful as antiseptics. After the upper bowel is free of fermenting contents, bismuth, chalk mixture, or other mild astringents may be desirable to allay existing irritation and check the tendency to further diarrhoea. Pancreon, prepared by treating pancreatin with tannin, is recommended when intestinal indigestion is due to decreased secretion of pancreatic juice. It is administered dissolved in water before meals in a dose of gr. vj (gm. 0.4). In cases in which gastric disorders have preceded the intestinal disturbance the treatment should be directed primarily to the condition of the stomach.



## INTESTINAL COLIC

**Definition.**—The term intestinal colic should be restricted to attacks of paroxysmal intestinal pain caused by violent tonic contractions of the bowel resulting from undue stimulation of the intestinal nerves or from obstructive conditions. The more or less continuous pain and tenderness of inflammation of the bowels or peritoneum, and the purely neuralgic pain (*enteralgia*, in the strict sense) should not be included under the head of colic.

**Etiology.**—The immediate cause of the pain of colic is the excitation of the intestinal nerves and the violent tonic contraction of the bowels caused by irritating intestinal contents or by obstructive conditions. The cases may be divided into those in which there is mainly functional disturbance and those associated with organic conditions.

**Colic Due to Functional Disturbances.**—Some persons are so sensitive that even when the food or other ingesta are wholesome, slight causes such as exposure to cold, fatigue, anger, fright, or other emotional conditions, occasion attacks of colic. It is probable that under these circumstances digestion and absorption of food products are interfered with, fermentation or putrefaction occurs, and irritation of the intestinal nervous mechanism takes place. More commonly, colic results from a definite error in diet. The eating of coarse foods, unripe fruit, indigestible substances of all sorts, especially if in excessive quantity, is perhaps the commonest cause. The drinking of cold water, beer, or other liquids at the same time may add to the disturbance, or may alone suffice to bring on an attack. Developmental conditions causing functional weakness or chronic conditions of the bowel, such as partial stenosis, may predispose to attacks of colic under relatively slight provocation, such as overeating. In infants or young children the connection between dietetic errors and colic is nearly always apparent. Frequently such coöperating causes as exposure to cold, fatigue, or emotional disturbances may play an important etiological part. Idiosyncrasy also contributes, some persons finding it impossible to eat certain, usually wholesome, articles of food without suffering an attack. Whether the ingested food is inherently irritating or is rendered so by the conditions of the patient at the time, or his idiosyncrasies, the result is a violent irritation of the nerves of the intestines and a forcible contraction of the muscles of the intestines which causes the painful paroxysms. If the amount of food residue and gaseous accumulations in the intestinal canal is excessive, the obstacle thereby offered to the contractions of the bowel becomes an added cause of pain. Nearly always some sort of obstacle to the free movement of intestinal contents is more or less responsible for attacks of colic. In some cases violent irritation of highly noxious substances may occasion a spasm or paresis of a segment of bowel which thus becomes practically a seat of obstruction. Mere distension of the bowel by gases does not occasion colicky pain, as may be seen in the comparative freedom from all pain in cases of quite marked meteorism and the different type of discomfort or pain in cases of excessive distension.

Certain special substances may act in a direct way upon the nervous mechanism of the bowel. This is seen in the intense colic of lead poisoning and the colicky pains caused by certain laxative medicines.

Formerly much was said about "rheumatic colic." The cases so designated were cases of colic following exposure to cold and associated with more or less muscular soreness. Some of these doubtless were simply instances of painful conditions in the abdominal walls; others cases of colic due to intestinal indigestion, fermentation, etc., following the eating of indigestible food, and exposure. It is doubtful if any of the cases were instances of "rheumatic colic" in a proper sense.

Fecal accumulations may cause purely functional colic, although they are usually associated with some organic condition. When a considerable impaction has occurred, the peristaltic efforts of the bowel above the accumulation become more and more severe until finally tonic contraction ensues and an attack of colic results.

**Colic Due to Organic Conditions.**—Foods may prove so irritating to the bowel that an actual catarrhal inflammation is occasioned. This happens quite frequently in children when tainted milk is taken and in adults when bacterial decomposition causes putrefactive changes. The catarrhal inflammation adds to the irritability of the intestinal nerves and increases the tendency to an attack of colic. Ulceration of various sorts of the large or small intestine, such as tuberculous, typhoidal, stercoral, or simple follicular, may occasion genuine attacks of colic. The association of colic with appendicitis is exceedingly common, and may be due to violent contractions of the appendix itself (appendicular colic) or the ileum or colon. All these inflammatory lesions may excite tonic peristaltic contractions, and the partial obstruction at the site of inflammation increases the obstacle to the movement of the intestinal contents from above.

**Symptoms.**—The ordinary attack of intestinal colic due to functional disorder of the bowels is usually sudden in onset, beginning with violent cramp-like pains in the umbilical region which spread in various directions. As the peristaltic movements advance from one part to another the patient experiences a change in the position of the pain, and there may be at the same time a sense of movement of gases from one coil of intestines to another. In very severe attacks the pain is more fixed and cannot be definitely localized. The patient at first moves from side to side, draws up his leg, and presses his hands or a pillow against the abdomen, and finally assumes a constant position with thighs flexed toward the abdomen. Pressure usually affords relief, but if inflammatory conditions of the bowel are present, pressure may increase the pain. In young children an attack of colic is indicated by crying, restlessness, drawing up of the legs, violent contractions of the facial muscles, and later by abdominal distension. Rumbling sounds or borborygmi may indicate the movement of gases in the bowels. Usually attacks of colic subside after a duration of from a few minutes to some hours, and when gas has been discharged or the bowels evacuated. In severe cases the attacks may continue unabated for several or many hours and the patient may grow faint or suffer partial collapse, breaking out into a

cold sweat and growing quiet from exhaustion. Severe attacks may also be attended with nausea and vomiting. The temperature is usually little altered, but a moderate degree of fever is not uncommon.

After relief from the primary attack, exacerbations and remissions may follow until the bowels have been thoroughly evacuated or the irritation otherwise removed. A certain amount of abdominal soreness and tenderness may remain after the attacks have ceased and a return to normal intestinal conditions may be delayed for several days.

The bowels at the onset of colic are usually constipated. When relief begins there is usually some discharge of flatus and evacuation of the lower bowel; later, a diarrhoeal condition may follow, particularly if catarrhal inflammation has accompanied the attack or occasioned it.

Attacks of colic in which the irritation has been sufficient to cause an inflammatory condition are more severe and lasting than those in which the derangement is only functional. Disturbances of the stomach, abdominal distension, soreness and fever are also more likely to occur in these cases; and after relief from the acute condition tenderness and pain, diarrhoea, and sensitiveness are apt to persist for some time.

Colic, associated with organic diseases of the bowels, such as intestinal obstruction from carcinoma, bands, internal hernia, fecal impaction, etc., will be considered in the discussion of those conditions.

*Enteralgia* or *neuralgia of the intestines* in the strict sense is a rare condition, and to be distinguished from colic by reason of the fact that it is probably not dependent on a tonic intestinal contraction, but rather on a direct painful irritation of the intestinal nerves. Such a condition occurs in hysterical persons and in association with tabes and other organic spinal diseases. The attacks are sudden and severely painful, but unattended with the usual indications of colic. There is intense sensitiveness on pressure, and relief occurs independently of evacuation of the bowels. The general appearance of the patient suggesting a neurotic origin of the pain is more or less characteristic.

**Diagnosis.**—It is often exceedingly difficult to determine the nature of an attack of abdominal pain having the general features of intestinal colic. The serious character of other conditions which simulate its features requires that these be carefully considered before an attack is regarded as simply intestinal colic. Among other conditions, biliary, renal, and uterine colic must be thought of; the similarity in the symptomatology of rupture of a gastric or duodenal ulcer must be remembered; and above all else, on account of its frequency and seriousness, appendicitis must be kept in mind. The last-named offers the greatest difficulty; but if local pain, tenderness and rigidity, fever, leukocytosis, marked gastric symptoms, obstinate constipation, disturbances of the pulse, and the general condition of the patient be carefully considered, a mistake in diagnosis is not likely to be frequent.

Certain less frequent conditions may require consideration. Among these, acute pancreatitis, the passage of a pancreatic calculus, embolism or thrombosis of the mesenteric vessels, and referred pains, such as those occasionally experienced in the abdomen in cases of thoracic



diseases, as pneumonia, pleurisy or angina pectoris, or in pelvic diseases, must be remembered. The onset of acute intestinal obstruction must be carefully distinguished. Usually the failure to relieve the attack by simple measures establishes the diagnosis. In cases of chronic intestinal obstruction the significance of attacks of colic may be overlooked. A partial obstruction may be unattended with marked symptoms until an attack of acute colic occurs. The possible association of this with a chronic condition must be remembered.

**Treatment.**—Intestinal colic readily subsides when the bowels are evacuated and the local irritation is controlled by various warm applications and by the use of sedatives. If the diagnosis is assured, the bowels may be emptied by the use of a large injection of warm water or soap-suds, to which castor oil or sweet oil may be added; or by the administration of a dose of castor oil if the stomach permits. Salines, calomel, or other purges may be used if the urgency of symptoms does not require speedier agents.

Small doses of opium or morphine not only allay pain but relax spasm, and thus sometimes aid in securing purgation. Various carminatives, such as spirit of chloroform, oil of peppermint, menthol, or camphor water may be combined with opiates, especially when gaseous fermentation is present. A prompt hypodermic injection of morphine, followed by measures to relieve the bowels, may cut short an attack of threatening severity. Local measures, such as hot-water bags, hot fomentations, poultices, etc., give relief, and by relaxing spasm may secure evacuation of the bowels.

In children, hot applications applied locally, hot baths, carminatives with paregoric, mild laxatives, such as castor oil with paregoric, magnesia, calomel, and enemata suffice for severe attacks, while the milder paroxysms are relieved by using soda-mint, oil of peppermint, aromatic spirit of ammonia, or Hoffmann's anodyne.

**Lead Colic.**—A peculiar form of colic is that which is met with in subacute lead poisoning, and commonly known as lead colic, painter's colic, etc. In this form the important symptom is intense cramp-like pain attended with obstinate constipation. The abdominal muscles are found rigid and contracted, so that the abdomen is flat or even hollow. Other indications of lead poisoning are commonly present, and a blue line along the edges of the gums where they join the teeth is almost pathognomonic. Paralysis of the extensor muscles of the forearm, causing the characteristic wrist-drop, may or may not be present. During the attack of colic the pulse has a peculiar wiry hardness, indicating a high tension, which has been ascribed to tonic contraction of the bowels and consequent increased resistance to the abdominal circulation.

**Treatment.**—This is directed to the relief of the symptoms and the elimination of lead from the system. In the early stages magnesium sulphate should be given freely for the double purpose of converting any soluble lead salts in the stomach or bowels into the insoluble sulphate and of relieving constipation. At the same time opium may be given by the mouth or rectum, or hypodermics of morphine may be used to

allay pain and relieve intestinal cramps and spasm. Free venesection gives prompt relief in some cases. Iodide of potash in doses of from 10 to 15 gr. (gm. 0.65 to 1) three times daily aids in eliminating the lead.

### INTESTINAL HEMORRHAGE

**Etiology.**—The causes of hemorrhage from the bowel are exceedingly numerous. In some cases this condition occurs without any definite organic lesion of the intestines; but more commonly, hemorrhage signifies some definite change.

**Hemorrhage Unassociated with Pathological Conditions of the Bowel.**—In association with certain hemorrhagic diatheses or diseases, such as purpura and scurvy, and in some infections, such as septicopyemia, yellow fever, and severe malaria, hemorrhage may occur without preceding alteration in the mucous membrane of the bowel. At the time of the hemorrhage, or before it sets in, extravasation of blood into the mucosa may occur; and the source of the hemorrhage may be such an area. Occasionally hemorrhages occur from the mucous membrane of the bowel without any discoverable lesion. Cases of this kind have been met with in tuberculous individuals by Nothnagel and others. It has been claimed that hemorrhages of this sort may take place as a vicarious manifestation of menstruation.

**Hemorrhage as the Result of Congestive Conditions of the Bowel.**—In cases of cirrhosis of the liver, valvular disease of the heart, and hemorrhagic infarction of the bowel following embolism or thrombosis of the mesenteric vessels, hemorrhage may result. Similarly, in cases of intussusception, strangulation of the bowel, or hernia, there may be hemorrhage as the result of overdistension of the bloodvessels.

**Hemorrhage as the Result of Diseases of the Bloodvessels.**—The most frequent cause of hemorrhage from the bowels is hemorrhoids. Other diseased conditions of the bloodvessels may, however, occasion hemorrhage. Thus in aneurismal dilatations of the hepatic artery, rupture may take place into the bile passages, and discharge of blood from the bowel may ensue. Similar conditions of the intestinal vessels occur more rarely. Amyloid degeneration of the intestinal vessels is a common cause of extravasation into the bowel in local or general amyloid disease. In grave anemias and in severe infections, degeneration and rupture of the bloodvessels may be the cause of enterorrhagia. Sometimes in the course of chronic interstitial nephritis considerable intestinal hemorrhage may occur, probably resulting from degeneration of the bloodvessels and increase of arterial tension.

**Hemorrhage as the Result of Inflammatory and Ulcerative Conditions of the Bowel.**—In cases of gastric and duodenal ulceration and in typhoid fever hemorrhage occurs frequently. Less marked hemorrhage often attends carcinomatous ulceration; while in ulcers of other sorts, loss of blood, although less marked and conspicuous, may be met with. In inflammatory affections of the bowel without ulceration, hemorrhage is much less commonly present. If, however, the inflammation is intense

and the congestion is marked, some loss of blood may occur, although free hemorrhage is unusual. Continued slight bleeding is caused by certain parasites, notably ankylostoma.

**Symptoms.**—Ordinarily, no difficulty occurs in the recognition of hemorrhage from the bowels, but it may be difficult to determine the source. As a rule, when the blood comes from the colon or rectum its color is a bright red, and on microscopic examination the corpuscles are well preserved. When hemorrhage occurs from the upper bowel, unless active peristalsis causes its rapid discharge, secondary changes are usually observed. The stools become dark and often tarry in appearance, and are usually highly offensive from decomposition. In many cases there may be a gradual loss of blood from the bowel of so slight a degree that a naked-eye inspection of the stools does not reveal any evidence of hemorrhage. In such cases an examination for occult blood may show its presence. In cases of larger hemorrhage a microscopic examination may discover crystals of blood-coloring matter and dark amorphous pigment. In cases in which inflammatory lesions, ulceration, and especially carcinoma, have occasioned hemorrhage from the bowels, the blood is often associated with mucus and pus, as well as with epithelial cells and other tissue elements.

Hemorrhage from the bowels rarely occasions pain. If the loss of blood is great, the symptoms are those of extensive hemorrhage from any source. After a hemorrhage, intestinal symptoms often develop as the result of putrefactive changes in the blood retained in the intestinal tract. Secondary diarrhœa may be set up as a consequence. Repeated small hemorrhages from the bowel may occasion extreme anemia.

**Prognosis.**—The result of intestinal hemorrhage depends entirely upon its cause. Severe losses of blood are, of course, in all cases serious; but sometimes very extensive hemorrhages are followed by no material impairment of the patient's health. In cases of hemorrhoids, as well as in cirrhosis of the liver or other obstructions of the portal circulation, actual improvement may be observed. Repeated losses of blood are of more moment; and when intense anemia has developed, the prognosis is always very grave.

**Treatment.**—This must always depend upon the cause, although certain general rules may be formulated. Local applications of cold, such as the ice-bag, Leiter's coils, and the like, are commonly employed, although their value is extremely doubtful. Injections of ice-water into the rectum and colon may, perhaps, be valuable in some cases of hemorrhage from these parts, but in other instances may be actually harmful, by stimulating the peristalsis of the bowel.

Colonic douches may be beneficial when the source of the hemorrhage can be reached in this way. Solutions of nitrate of silver, tannic acid, or other astringents, may be employed. If the hemorrhage cannot be reached, such injections, however, may be objectionable; because, by irritation, they may stimulate active peristalsis and renewed hemorrhage.

*Opium* has been universally employed for its effect in controlling peristalsis and quieting the patient. The judicious use of this drug is advisable in some forms of intestinal hemorrhage, but it should not be



used to such an extent that the bowels are completely locked and the blood and other materials therefore retained and permitted to undergo putrefactive decomposition. Astringent remedies, such as nitrate of silver, acetate of lead, bismuth salts, and tannic acid preparations, are sometimes useful. Other hemostatics, like chloride or lactate of calcium and gelatin, may be used. In the case of the latter, peristalsis should not be checked, so that the gelatin may reach the bowel in an undigested form. Ergot, hydrastis, and turpentine are of doubtful value.

## CONSTIPATION

**Synonyms.**—Habitual constipation; obstipation.

**Definition.**—Infrequency in the evacuation of the bowels and a tendency to abnormal dryness or hardness and reduction in the quantity of the feces are the conditions comprised in the term constipation. It is difficult to give a positive definition, since the physiological limitations vary widely. In most healthy persons there is normally an action of the bowels once in twenty-four hours, and when the conditions of life are uniform this occurs at approximately the same time of day. When the intervals are two or three days, even though symptoms are absent, the condition must be regarded as one of constipation. Instances, however, have been reported, such as the cases of Reichmann, in which there was but one movement in two or three weeks, the patients in the meantime presenting no symptoms of disease. Such cases must be regarded as cases of decided constipation. Sometimes, although the movements occur daily, the quantity is decidedly below normal and the character of the movements inspissated. In other cases, by testing with charcoal or carmine, it may be found that, although an approximately normal movement is evacuated daily, the duration of time in the intestinal tract has been prolonged, so that considerably more time elapses between the ingestion of food and the discharge of the residue than occurs in normal individuals. This has been defined as latent constipation. Essentially, then, delay in the evacuation of food residues and abnormal inspissation, with a reduction in the quantity of the excreta, constitute the condition under discussion, whether symptoms be present or not.

Recent authorities tend toward the limitation of the term to purely functional conditions, excluding cases in which organic disease of the bowel is present. This cannot, however, be fully accomplished; for such conditions as ptosis of the transverse colon, movable cecum and redundancy of the sigmoid are often encountered in cases admitted under the chapter on Habitual Constipation, and other minor intestinal lesions cannot be excluded, though it is fully understood that constipation resulting from definite intestinal diseases (adhesions, strictures, etc.) is to be considered as merely a symptomatic result of such disease.

**Etiology.**—Any discussion of the causes of constipation must be based primarily upon a knowledge of the physiological processes concerned in the onward movement of the intestinal contents. These processes are more fully described in the section on Physiology of the

Intestinal Tract. It will be sufficient here to note that the efficiency of the peristaltic movements will depend upon the normal strength of the muscles of the bowel, the integrity of the nervous mechanism, the amount of residue in the intestinal contents and the character of the contents. Solid contents, water and other liquids, or gases, may serve as stimulants either mechanically or chemically. Sometimes the irritation results from the mere bulk of the contents; more commonly, the mechanical nature of the contents determines their effect. Thus, coarse and irritating substances and insoluble residues of various sorts are particularly exciting. Of gases, hydrogen, oxygen, and nitrogen are said to be indifferent, while carbon dioxide, sulphuretted hydrogen, and volatile hydrocarbons stimulate activity.

The onward movement of the residual matters left in the bowels after complete digestion is the result of the peristaltic movements. Through this agency the contents traverse the small intestine in the course of a few hours and the large intestine in from twenty to twenty-four hours. The slower progress in the colon is probably the result of the frequency of antiperistaltic waves, which Cannon has found to be the prevalent form of motion in this portion of the intestinal canal.

The final evacuation of the feces is caused by reflex stimuli produced by irritation in the rectum resulting from the presence of feces and the direct voluntary expulsive efforts which involve contractions of the abdominal muscles. The preservation of a normal rectal reflex is of the greatest importance and its loss or diminution is the important factor in certain cases of constipation.

The condition of the abdominal muscles plays a further part in the whole process of the movement of the intestinal contents in that the condition of these muscles and the effect of their normal contraction influences very largely the activity of the peristaltic contractions of the intestines. The integrity of the abdominal muscles is of course highly important also in the act of defecation.

It will be seen that abnormal sluggishness in the movement of the contents of the bowels may be the result of (1) the character of the food residues; (2) weakness of the intestinal muscles; (3) weakness of the nervous mechanism; (4) weakness of the abdominal walls.

In addition to the causes of reduction in the normal motor function it seems probable that abnormalities in the absorption processes may be of importance. Some authors (Schmidt) insist that there is excessive digestibility of cellulose as a result of which this most important stimulant to peristaltic activity is withdrawn. Others have suggested that rapid absorption of water and premature inspissation of the feces in the upper part of the large intestine is an important factor.

Finally, perverted intestinal contractions causing spasms of localized or considerable portions of the lower bowel or, on the contrary, segments of partial or complete atony, may prevent the onward movement of the fecal matters.

**Functional Causes.**—There may be considered under this head conditions which produce torpor of the intestines themselves and conditions which cause a weakness of the diaphragm and abdominal walls, and

thus lead to reduction in the expulsive power or indirectly to weakening of the intestines themselves. We may also include causes of spasm of the bowel or of abnormal absorption.

Intestinal torpor may occur acutely and as a result of various nervous conditions. Thus, as a result of fear or other emotions and nervous manifestations in neurasthenia, melancholia, and the like, intestinal atony and constipation are not infrequent. Frequently this torpor results from habit. The normal individual tends to evacuate the bowel after the first meal of the day, probably for the reason that at this time the food residue of the previous day has reached the lower bowel and that the ingestion of food into the stomach, together with the change of position of a person from the recumbent to the upright, and the exercise taken up with the day's work, excite peristaltic contractions and the tendency to evacuation. When, as a result of lack of time or inattention, this stimulus is ignored or resisted, the desire passes, and with repetition of such neglect the habit of longer retention is established. The normal stimulus from the lower bowel becomes less and less effective, and eventually a state of chronic constipation results. Long retention of fecal matter in the lower bowel has the further unfavorable effect of causing dilatation of this portion of the bowel and an active organic weakening of its expulsive power. In individuals suffering from long-continued constipation, considerable pouching of the sigmoid, descending colon, and rectum is not infrequent. Certain authors have assumed that there is some special form of weakness of the innervation of the muscles, especially of the colon and rectum, but fail to make clear the manner of its occurrence. Similarly it may be assumed that in certain persons there is some inherent weakness of the intestinal musculature.

Diseases of the stomach frequently occasion chronic constipation. In some instances this may be the result of the long retention of food in the stomach owing to the reduction of its motor power or obstruction of the pylorus, and possibly stimuli normally propagated from the stomach to the intestine fail to be generated. In addition, the contents of the stomach may be transmitted to the intestine in such condition that irritation of the bowel is first produced, and later spasmodic or tonic contractions which cause the resulting constipation.

The *dietetic* causes are numerous and most important. The habitual use of food which leaves little residue is a very frequent cause. The constipating effect of a milk diet is thus explained. Similarly, the use of highly concentrated food, such as meat, eggs, etc., with little addition of such substances as vegetables, which contain a relatively large amount of unabsorbable residue, may produce habitual sluggishness of the bowels. The neglect of vegetables, besides causing a reduction in the amount of residue, has the disadvantage of removing from the dietary a large proportion of the neutral salts which are normally active in regulating the action of the bowels. Occasionally the bowels become constipated as a result of the eating of foods which contain an excess of irritating residue, such as berries containing small seeds or vegetables rich in cellulose. This form of constipation is due to spasmodic conditions of the bowel caused by the excessive irritation. In many persons



the cause appears to be insufficient use of water, and the resulting dryness of the intestinal contents; or the drinking of hard water containing large quantities of lime salts may be at fault.

*Bacteria* play an important rôle in the normal as well as in the abnormal conditions affecting the intestinal tract. The number of bacteria in the feces of constipated persons is decidedly smaller than in those of normal individuals. This is, in part, due to the fact that the sluggish peristalsis occasions a longer retention of food in the bowel, and consequently a fuller degree of absorption of the nutritious element. As a result, the bacteria which mainly flourish in the lower intestinal tract are deprived of pabulum and multiply less freely, in consequence of which fatty acids, gases, and other products of bacterial growth are wanting and the stimulus to peristalsis normally exercised by these products is lacking. To some extent the bacteria also excite mucus formation in the normal bowel, and this aids as a lubricant and helps to keep the feces soft.

Congestion and inflammation of the bowels in certain cases cause constipation by directly weakening the contractions, but this mode of causation is probably far less frequent and important in genuine habitual constipation than was at one time assumed. It would appear that chronic constipation is more usually the result of disorder of the nervous mechanism which controls peristalsis than of any direct weakness of the wall of the bowel. It cannot be denied that inflammation or congestion, and especially such conditions as congenital or acquired dilatation of the bowel, may produce constipation by direct weakness of peristalsis, and it is contended only that such factors are of relatively little importance compared with reduced motility through alterations in the contents of the bowel or of the neuro-muscular mechanism.

Various causes operate to produce constipation by causing weakness of the diaphragm or the abdominal walls. A direct effect is probably exerted upon the movements of the intestine by the contractions of the abdominal muscles, and it is probable that a normal condition of tone in the abdominal walls has a certain reflex influence in producing a like state in the underlying organs. Furthermore, relaxation of the walls of the abdominal cavity allows of dilatation of the contained hollow viscera, which interferes with the effectiveness of the contraction of these organs. Clinically, it is certain that various conditions which cause weakness, either of the diaphragmatic movements or of the abdominal parietes, occasion sluggishness of the bowels. Thus in chronic diseases of the chest, such as emphysema, pleural adhesion, etc., more or less obstinate constipation may occur. The effect of weakness of the abdominal walls is evident in the constipation that occurs after repeated pregnancies or when large accumulations of fat have been deposited in the omentum or abdominal walls, or in the case of various abdominal tumors. Intestinal sluggishness may reach high grades in cases of decided separation of the recti as a result not only of the weakness of the superficial structures but also of displacement of the intestines (enteroptosis).

Dress probably has a certain amount of influence as a cause of constipation. The much greater frequency of this disorder in women than

in men may be attributed to lack of equal exercise, to the more frequent neglect owing to inconvenience of surroundings, etc., and possibly to certain anatomical considerations; but it is not improbable that the character of clothing has something to do with this greater prevalence in women. The weakness of the abdominal walls which results from constriction of the lower chest and abdomen may quite readily serve as a contributing cause.

*Sedentary life* and lack of exercise operate in a variety of ways. In the first place, there is a tendency to digestive disturbance and a lack of general systemic tone, and in a more direct way these conditions may operate by producing weakness of the abdominal muscles. Some individuals normally perfectly regular become constipated when confined to the house or room by some trivial ailment which merely restricts the usual exercise. The same result also occurs to persons on long railway journeys or sea voyages, and the like, and is especially marked in patients confined to bed through some injury or a disease not necessarily affecting the abdominal walls directly.

**Organic Causes.**—More attention was formerly paid to the importance of strictly organic conditions in the development of habitual constipation than is now given to such conditions. Undoubtedly adhesions or partial obstructions by stenoses of localized segments of the bowel or constricting bands surrounding a coil of intestine may be the occasion of intense and long-continued constipation. Similarly, uterine displacement, pelvic tumors, malpositions of the intestine (enteroptosis), or congenital or acquired malformations (idiopathic dilatation of the colon) may be of importance in certain instances. Likewise, certain conditions affecting the efficiency of the expulsive efforts, such as a weakened perineum from lacerations, and diseased conditions or relaxation of the abdominal walls, may be of some influence. It is difficult to determine how far the term habitual constipation may be extended to include such organic conditions. As has been stated before, those who contend rather insistently for the limitation of this term to functional conditions do not exclude ptosis of the transverse colon, which in a sense acts as an organic or mechanical cause of delayed peristalsis and of onward movement of the intestinal contents quite as much as adhesions.

**Functional Types of Constipation.**—Attempts to divide cases of constipation into different types have not been specially satisfactory, but something is gained by recalling such classifications.

(a) *Atonic Constipation.*—It is generally admitted that atonic conditions are the prevailing fault. We may include here various causes of intestinal torpor such as that due to dietary errors (alimentary constipation) to general or local weakness, to habits of irregularity of defecation and reduced form of expulsion, etc.

(b) *Spastic Constipation.*—As a result of irritable conditions of the bowel itself or reflexly, localized or extensive spasms, sometimes shifting, sometimes more fixed in location may occur.

**Fluoroscopic and Skiagraphic Findings.**—A study of the movement of the intestinal contents in cases of constipation usually shows but little retardation of the passage through the small intestine, though the

complete emptying of the small intestine may be manifestly delayed. In the large intestine there is a distinct delay which may be most manifest in different localities in different cases. In some the bismuth accumulates in the cecum and very little, if any, reaches the hepatic flexure at the expiration of eighteen or twenty-four hours; in others, especially when there is decided ptosis of the transverse colon, the most marked delay is seen in this portion; in a third group the delay is evidently most marked in the descending colon or sigmoid flexure. In cases of spastic type affecting the descending colon or sigmoid the skiagram of these portions may plainly indicate the narrowing of the contracted bowel. When constipation is largely the result of retention in the rectum and reduced expulsion enormous enlargement of the rectum may be seen.

**Pathology.**—In a majority of cases but little structural alteration can be detected. Certain resulting conditions are met in a certain number of the cases. Nearly always there is some abnormal distension of the sigmoid and rectum, and when constipation has been extreme and its duration prolonged, distinct pouches or diverticula may be produced. In some instances these will be found to contain hardened scybala and inflammatory materials, and even ulceration of the mucous membrane may occur (stercoral ulceration). Hardened scybala may produce severe catarrhal inflammation of the mucous membrane.

Marked distension of the colon, with thinning of the mucous membrane and of all the walls, may result from obstinate constipation, especially when accompanied by frequent impactions in the lower bowel. The small intestine rarely shares in such distensions. More commonly there may be narrowing of the lumen and thickening of the wall in limited segments due to long-continued or repeated spasmodic contractions, especially in cases in which habitual insufficiency of food has been a principal cause. The writer has repeatedly met with such contracted areas of the bowel in autopsies in cases of chronic insanity in which there has been long-continued insufficiency of food and resulting constipation.

Sometimes infiltration of the inspissated fecal masses or scybala with salts of lime or magnesium may result in the formation of so-called "coproliths." These are always found in the large intestine.

**Symptoms.**—The important symptom of constipation is the infrequency of evacuation or the inspissated character and reduced amount of feces. There is usually a tendency to the formation of hardened masses or scybala. The act of evacuation is attended with difficulty and not rarely with a certain amount of local pain. When the condition is long continued and the masses are of unusual hardness, some mucous coating and even blood-streaked mucus may be observed. If the lower bowel has become impacted, cramps or colicky pains may, for some time, precede the evacuation. Not rarely a certain amount of tenderness is found in the left iliac fossa over the sigmoid flexure.

Various subjective symptoms are met with in persons suffering from habitual constipation, and it is at times difficult to determine how far these have resulted from the condition, or, on the other hand, the degree in which they may have acted as causes of the sluggishness of the bowel. Among such symptoms, heaviness, sleeplessness, a tendency to vertigo,



headaches, and even more severe nervous symptoms, like hypochondriasis, may be mentioned. Undoubtedly all of these may be occasioned by the existence of obstinate constipation, but, on the other hand, sluggishness of the bowels is frequently the result of such nervous conditions and perhaps more remotely of the gastric disorders that have occasioned these symptoms. Some authors have suggested that neurasthenia is frequently caused by atonic conditions of the bowel, with more or less constipation, but more commonly constipation is rather a symptom of the neurasthenia than the reverse.

Local abdominal symptoms are common and significant. A feeling of fulness or of pressure, a sense of distension, and sometimes vague or acute pains may occur. Pain may be localized to regions where accumulated masses of hardened feces have caused irritation or inflammatory conditions. In other instances cramp-like colic affecting the region of the descending colon or the entire abdomen may result from impaction and from the resulting stimulation of violent peristalsis.

Rectal impactions occasion sensations of bearing down or perineal fulness and even violent tenesmus. Secondary disorders of digestion, with loss of appetite, coating of the tongue, sleepiness, thirst, and sometimes more acute symptoms, such as nausea and vomiting, may, from time to time, make their appearance or be more or less constant.

*Fever* not infrequently occurs, when the degree of constipation is temporarily more marked than usual. This may be the result of the direct irritation of retained masses of hardened material or may possibly be the consequence of the absorption of products of decomposition (stercoremia). The evidence in favor of the latter is rather insufficient, as the indications of intestinal fermentation or putrefaction are rarely marked in constipation, and other signs of toxemia are wanting. In the great majority of cases of constipation fever does not occur.

Local disorders of various sorts may be encountered, such as palpitation of the heart, irregularity of cardiac action, and various nervous symptoms, some of which have been already mentioned. These symptoms, like fever and cerebral manifestations, have been attributed to auto-intoxication, although the evidence in favor of this view is scanty and uncertain.

The abdomen is sometimes flat or even scaphoid from general contraction of the intestines and insufficiency in the contents of the bowel. More frequently there is slight distension with excess of tympany in the sides due to dilatation of the large bowel. When the abdominal walls are weak and thin, the dilated colon may be seen almost throughout its entire course. Hardened fecal masses may be palpable through the abdominal walls, especially in the sigmoid region. The character of the masses is recognized by their movability, by their disappearance after purgation or the use of enemata, and, according to Gersuny, pressure upon the fecal tumor causes a characteristic sensation of separation of the wall of the bowel from the tumor when the pressure is relaxed. Sometimes fecal accumulations occur in the transverse colon or even in the cecum, and may be very misleading in their resemblance to abdominal tumors.

Occasionally attacks of *diarrhœa* may occur in persons subject to

habitual constipation. Such attacks may result from irritation caused by impaction or excessive retention of the intestinal contents from food irritation, or other forms of irritation (purgatives), which act excessively on account of the retention of fecal matter and its hardened character. In cases of fecal impaction in the rectum the real condition may be obscured by a continuous diarrhœa caused by irritation.

The general condition of the patient suffering with habitual constipation may not be seriously impaired. In some cases, however, emaciation, loss of strength, and some anemia may result from the gastric disorders that usually attend constipation, from the constant use of purgative medicines, and possibly from obscure toxic conditions.

**Complications.**—Among the intestinal complications are dilatation and pouching of the rectum and sigmoid flexure, formation of diverticula, volvulus, and inflammatory lesions in various parts of the bowel (rectum, colon, appendix). Constant straining in constipation may lead to weakening of the abdominal wall and to the formation of hernia. The same cause, together with the pressure of masses accumulating in the rectum and the direct irritation occasioned by hard scybala, frequently leads to the development of hemorrhoids. Severe straining sometimes occasions thoracic diseases, such as emphysema of the lungs. Apoplexy may result from the elevation of blood-pressure caused by severe straining.

**Diagnosis.**—This usually offers no difficulty whatever, as the infrequency of the evacuations and their character are distinctive. Sometimes, however, there may be daily evacuations of comparatively normal amount, and apparently normal in other respects, in which a physiological test made with the use of charcoal or carmine will show that the time that elapses between the ingestion of a certain meal and the discharge of the residue is considerably prolonged. The recognition of such cases might prove difficult, if one did not recognize the possibility of such an occurrence. Fulness of the abdomen, general sluggishness, a tendency to headaches, digestive disturbances, oppression, and other similar indefinite symptoms, may suggest the existence of such latent constipation; and this may be suspected, also, in cases in which there is visceroptosis.

Another direction in which the diagnosis of constipation frequently offers difficulties is in the determination of the cause of the condition. The existence of distinct gastric symptoms antedating the tendency to constipation may suggest that digestive disturbance is mainly operative. A study of the patient's diet may bring out that a too monotonous diet, or one lacking in fluid elements, or, on the other hand, foodstuffs that by irritation provoke intestinal spasm, lie at the basis of the condition. The condition of the abdominal walls, a tendency to gaseous distension, and other indications of sluggish peristalsis, may show that constipation has resulted from intestinal atony. Hemorrhoids or fissure, pelvic diseases, displacements of the uterus, or the presence of abdominal tumors, may indicate that the disorder has resulted from reflex atony or spasm of the bowel; or, in other cases, from direct pressure upon it. Finally, general nervous conditions, such as neurasthenia or other depressive conditions, may suggest the importance of the nervous system

in the etiology. In these instances careful consideration of the possibility that the nervous conditions are secondary to the constipation must be remembered in attempting to determine the sequence of events.

No satisfactory treatment can be instituted until the proper causation has been investigated and determined.

**Treatment.**—The most important element is the establishment of the habit of regularity in the evacuation of the bowels. The normal regularity of evacuation is due to the fact that the residue of food and the admixture of bacteria and secretions which constitute the feces reach the lower bowel at a certain interval after the ingestion of food, and there stimulate the mucous membrane and bring about a desire for evacuation. A habit of resisting this desire may gradually cause a blunted sense, which eventually occasions more or less obstinate constipation. A process of reëducation is frequently effective, and the most natural and desirable method of treatment in the condition is the establishment of a habit of regularity. For some time no result may be achieved, but by repeated efforts at a certain hour—preferably that which seems to be the normal time (that is, the morning)—will gradually prove effective. In some cases it seems desirable to choose the evening rather than the morning, especially when local rectal conditions, such as hemorrhoids, are present. In these circumstances the retention of fecal matter in the lower bowel during the night may occasion a reflex spastic constipation.

Simple measures may be used to supplement the effort at reëstablishing the normal regularity. Among these the use of small enemata of plain water or soapsuds, with or without the addition of a little glycerin, and glycerin, gluten, or soap suppositories, may be recommended. All such aids should be used with caution, as the bowel readily accustoms itself to artificial assistance.

**Exercise.**—The condition of the abdominal muscles was referred to as being important in maintaining regularity. The constipating effect of enforced rest in bed, or of an enforced sedentary life in those who have before been regular, indicates the importance of this factor. Exercise of the abdominal muscles in particular is important, although the muscular system as a whole must be considered, since its normal healthful condition has a bearing upon the function of the bowels as on other visceral functions. The form of exercise must vary according to the physique, character, and occupation of the patient. In many, the institution of gymnastic movements and the use of pulley weights, rowing machines, or other apparatus that will enable the patient to obtain vigorous exercise, particularly of the muscles of the abdomen and trunk, answer the purpose. In others, a better result is accomplished by directing the patient to occupy himself with such labors as will secure the proper amount of exercise. In obstinate cases, passive exercise or massage must be employed. The patient may knead the abdominal muscles in the direction of the large intestine, or may use a cannon ball covered with felt or leather, which is rolled about the abdomen in the same direction as that used in massage. The weight of the ball may vary from two or three to ten pounds. Various implements have been devised for producing vibrasage, and these may give useful results in the treat-



ment of constipation. Active stimulation over the head of the colon and sigmoid, and a continuous treatment along the line of the large intestine, will give the best results.

A skilled manipulator combines all these forms of exercise by using stroking, kneading, and rotary movements and vibrations on the points indicated or along the entire length of the colon. Sometimes it is well to combine with the manipulations of a masseur high injections of plain water, which still further stimulate intestinal contraction.

Electricity and hydrotherapy have been used to supplement exercise or other forms of direct treatment. A slowly or rapidly-interrupted faradic current may be applied over the colon, beginning at the cecum, and following the entire length of the large intestine. Galvanism has also been employed, the current being interrupted from time to time. Ordinarily one electrode is placed under the back, while the other is applied to the surface of the abdomen.

Baths of various sorts have been employed to stimulate the abdominal muscles, as well as the intestinal peristalsis. Cold douches, wet compresses to the abdomen, and general hydrotherapy may be useful.

**Diet.**—It is impossible to make any general statement regarding the character of diet that should be prescribed for patients suffering with this condition. In general, it may be said that such forms of food as furnish a considerable amount of residue are likely to prove useful, while those foods which are susceptible of complete digestion and absorption tend to occasion constipation if they form too large a proportion of the whole dietary. It has, therefore, become customary to prescribe for patients with constipation various vegetable foods that leave a large residue. Other things bring equal, this plan proves satisfactory; but sometimes unabsorbed portions of food may act as irritants and tend to increase rather than to counteract the condition. In the same way, fruits, berries, and the like, which contain seeds or other non-absorbent constituents, may be helpful or hurtful, according to the nature of the case. All kinds of fruits have been advised, and frequently aid in combating the trouble. Sometimes, by causing disturbance of gastric digestion, fruits may have an opposite effect. Sweets, honey, milk-sugar, and other saccharine or carbohydrate foods sometimes prove efficacious. Stewed fruit at night, or a few dried plums, may have a useful effect. Milk-sugar has been largely employed in the same way.

In some cases the regular administration of water in increased amounts, and especially one or two glasses of warm or cold water in the morning before breakfast, may be helpful. Certain inert substances, such as agar-agar, which swells from imbibing water and is not digested or absorbed, liquid paraffin or petrolatum, are sometimes added to the diet with advantage. The regular use of olive oil in doses of from a teaspoonful to an ounce after each meal acts somewhat similarly. Various kinds of bread made of coarse flour or containing bran may aid by supplying a certain degree of desirable irritation. Certain foods have a recognized constipating effect. Among other things, acid wines or tea, on account of the astringent effect of the constituent tannic acid, are undesirable. Milk is usually constipating, but only when it forms a

considerable portion of the whole diet, and when, as a rule, the amount of residue left after digestion is inconsiderable and insufficient.

**Medical Treatment.**—Medicinal agents should be used in the treatment of constipation only when a regulation of the daily life of the patient, or of his diet, and the employment of various physical means of stimulating peristalsis have failed of the desired result. Undoubtedly, the common cause of increasing constipation is the employment of remedies without reference to the individual conditions, and usually without medical advice. Often, however, some kind of direct medical treatment seems necessary, and drugs may be required. These may be divided into those which exercise a helpful influence on digestion and peristalsis, without having a direct laxative effect, and those which are laxatives in a narrower sense.

Among the remedies that are correctives of digestion and stimulate peristalsis without irritating, *nux vomica*, *belladonna*, *physostigma*, and digestive ferments may be considered. Recently a preparation made from gastric mucosa and spleen, called hormonal, has been recommended for hypodermic administration as a peristaltic stimulant or hormone. Its usefulness and safety are still in question. In some cases a small dose of tincture of *belladonna* may suffice to aid the condition.

Of the direct laxatives, *aloes* and *cascara* are probably most generally useful. The well-known combination of *aloes* with *belladonna* and *strychnine* in pill form, to be taken at night, is useful, and if carefully controlled by other measures rarely requires such increases in the quantity of the remedies as to make it distinctly undesirable. *Aloes* may also be combined with *podophyllin*, extract of *rhubarb*, or *cascara*. *Cascara*, in the form of the fluid extract or solid extract, or of various elixirs, is a favorite remedy, and, like *aloes*, does not seem to increase the tendency to constipation. It is difficult to determine without experiment the required dose, individuals differing very widely in this respect. The combination with *aloes* or other purgatives often acts more happily than the drug without addition. *Phenolphthalein* is often useful and may be given with *cascara*.

*Senna* is a remedy widely used in domestic practice, and forms the basis of many proprietaries. An old practice used in many institutions is to administer stewed prunes, to which a few leaves of *senna* have been added; and *senna* teas, decoctions, etc., are extensively used. The official confection of *senna*, or one containing *senna*, *rhubarb*, *sulphur*, and *glycerin*, taken before bedtime, may be used. *Sulphur* may be used as a laxative, although its potency is rather limited.

Saline waters of various sorts, such as those of *Marienbad*, *Carlsbad*, *Bedford*, or *Saratoga*, may be useful. One or two drams of saturated solution of *magnesium sulphate* or *Rochelle salt* have a similar effect. As a rule, these waters are most efficacious when taken before breakfast or at night. The continued use of waters in regulated amounts may have a permanently useful effect, correcting digestion or catarrhal conditions of the gastro-intestinal tract, but the unrestricted use of any kind of saline water must be condemned.

Rectal medication is often highly beneficial, and in cases in which

some form of remedial agent seems to be necessary, the substitution of enemata, suppositories, etc., for remedies given by the mouth has the effect of preventing the development of a habit. The habit of employing enemata regularly or daily is quite common with some persons. It is not harmless, as the effect upon the mucous membrane of the lower bowel sometimes proves distinctly deleterious. As temporary expedients, enemata of plain water, saline solution, soapsuds, or more powerful combinations, such as solutions of sulphate of soda, Rochelle salt, or other salines, may be employed. In some cases, the injection of a small quantity of olive oil at night, to be retained until morning, has a useful effect, particularly in cases in which larger enemata are irritating. In cases of spastic constipation, such injections of oil or enemata of large quantities of oil may be employed. The addition of glycerin to enemata renders them more powerful, and specially efficacious in acute cases.

Sedatives may be useful in the treatment of constipation when the condition is more or less dependent upon spastic states of the bowel. In these circumstances the milder sedatives, such as bromides, valerian, and especially asafetida, given in the form of pills, each containing gr. ij, or administered by enemata in the form of milk of asafetida, serve a useful purpose.

Some attempts at correcting constipation due to a deficiency of microbic action have been made by the employment of cultures of microorganisms, such as lactic acid bacilli, etc. These methods have not proved especially valuable.

**Surgical Treatment.**—Attempts have been made to correct constipation by eliminating the large bowel from the intestinal tract. Among others, Lane has practised anastomosis of the small intestine with the sigmoid flexure or the rectum. Complete removal of the large intestine has been practised, but is obviously too radical a procedure to warrant recommendation. Even the more conservative forms of surgical treatment are justifiable only in cases of unusual obstinacy.

### IDIOPATHIC DILATATION OF THE COLON

This term is used to define certain cases of more or less extensive and persistent dilatation of the colon, probably dependent upon structural abnormalities, and not due to ordinary obstructions and to consequent accumulations of gaseous or fecal contents. The cecum, colon, and sigmoid may be enormously distended throughout their entire lengths. In some cases, however, the sigmoid alone is involved, and may be so greatly enlarged that it fills the entire abdominal cavity, pressing other viscera out of the way. The diameter of the bowel may reach as much as eight to ten inches. When the colon is involved, the abdomen is filled with the enormously distended ascending and descending colon, occupying either half of the abdominal cavity, which itself is so greatly enlarged that the patient presents the appearance of a monstrosity. Formad's celebrated case has been exhibited in various places under the name of the "balloon man."



**Etiology.**—A distinction may perhaps be made between cases in young children and those met with in the elderly or aged. The former group probably represents cases in which some congenital defect has been the occasion of the dilatation, which gradually progresses until the patient succumbs. In the cases occurring after childhood, contributing causes, such as partial obstruction, habitual constipation, and weakening of the bowel by chronic inflammatory affections, probably more frequently play a part. In a case reported by Treves the dilatation was due to congenital narrowing of the rectum; and this author concluded that idiopathic dilatation is usually due to obstruction with resulting fecal impaction. This view has not been sustained by later investigations, such as those of Crozer Griffith, who analyzed the post-mortem findings in eighteen cases in children. Marfan suggested that a congenital abnormality in the form of the sigmoid flexure might be the cause, and a number of cases have been described in which the sigmoid was abnormally long and therefore distorted. Other causes of impediment in either the sigmoid or the rectum may occasionally play some part in the causation. Some form of muscular weakness of the entire bowel has also been assumed as the basis; but idiopathic dilatation is not the result merely of atony of the bowel, as the walls are invariably found hypertrophied.

The important features are the great distension, a thickening of all the coats of the bowel, and especially hypertrophy of the muscle. The mucosa is usually swollen, congested, and ulcerated. As a rule, it contains large quantities of fecal matter; in Formad's case the contents of the colon weighed forty-seven pounds.

**Symptoms.**—The most conspicuous feature is the abdominal enlargement, which, on examination, proves to be due largely to gaseous contents. The distension may be uniform and globular, or may be more decided on one side—particularly on the left side—when the sigmoid is specially involved. The coils of intestines may be visible through the abdominal wall, and peristaltic waves may be seen. Interference with breathing and with the circulation is commonly the result of the upward displacement of the diaphragm. The patient complains of abdominal distress, but acute pain is usually wanting. Gastric disturbances, headaches, and intense constipation are usually encountered. Sometimes there are paroxysms of colicky pain, and occasionally attacks of diarrhœa may set in, especially toward the end of life. In some instances the bowels have been regular throughout, although there was nevertheless a gradual accumulation of retained fecal matter. The patient suffers with increasing malnutrition, which finally may become extreme; and death may be due to inanition and exhaustion. In other cases a fatal termination is due to volvulus of the sigmoid or to perforation of the bowel. Sometimes the fatal result appears to be due to the extensive associated colitis.

The clinical course in *congenital* cases begins within the first few days of life. The abdomen begins at once to enlarge, and increases progressively. At the same time, obstinate constipation attracts attention, practically no fecal matter being discharged, except at long intervals.

In some cases a history has been obtained that the child had had but few bowel movements since birth, although some months or a year or more old. The child usually dies early; in Griffith's series only three out of twenty-four cases reached adult years. In other cases the symptoms do not begin until a year or more after birth. Milder forms and sometimes even extreme cases may go on to adult or middle life.

**Treatment.**—In some cases the administration of purgatives may cause evacuation of retained contents; but this is followed by a speedy recurrence of the condition, and is attended with little relief, even for a time. The same unsatisfactory result attends the use of enemata. In a number of cases surgical treatment has been employed, and in a few has been followed by satisfactory results. The operation most generally employed has been colostomy, which in several cases has been quite successful. More extensive operative procedures, such as excision of parts of the bowel, have been resorted to with variable results. Richardson's case, in which excision of the sigmoid flexure was followed by the formation of a new sigmoid, is instructive in illustrating that inherent structural defects may lie at the basis of the etiology in some instances. Probably in most cases operation has been undertaken at too late a day.

## DIARRHŒA

**Definition.**—The term diarrhœa is usually applied to the too frequent discharge of more or less fluid stools. In many persons two or three daily evacuations of the bowels occur without disturbance of health, and without any marked alteration in the character of the feces from the normal. This does not constitute diarrhœa in the ordinary acceptance of the term. Usually, however, when more than one daily movement occurs, the feces are also less solidified; and although active symptoms may be wanting, the condition is really diarrhœa.

**Etiology.**—As the essential condition is the presence of an abnormal amount of water in the feces, the causes will be found to be such as occasion the rapid evacuation of the intestinal contents, with consequent reduction in absorption or an oversupply of water or increased secretion from the mucous membrane of the bowel.

The forms of diarrhœa may be classified as those without definite organic lesion and those associated with various intestinal diseases. In the latter group the condition is symptomatic, and more appropriately considered in connection with the various diseases that cause it.

**Diarrhœa Due to the Excessive Ingestion of Water and Other Fluids.**—Sometimes the mere drinking of excessive quantities of water may be the cause of looseness of the bowels. In some individuals in whom there is normally a constipated condition excessive water drinking may correct the difficulty or even produce a temporary diarrhœa. The drinking of other fluids, such as wines, malt liquors, etc., may act in the same way, although there is probably here an associated cause, the digestive disturbance resulting from the overuse of the fluids named. Diarrhœa is sometimes produced by the use of large quantities of oil, butter, or fatty

food. In this case the amount of unabsorbed fat may occasion looseness, or digestive disturbance may result from the excess of fat consumed, and the fatty acids or other products of decomposition may act as irritants.

**Diarrhœa Due to Food.**—Various foods may occasion diarrhœa, through their mechanically irritating character, through their ready decomposition in the gastro-intestinal tract, and sometimes through their mere bulk. It is well known that fresh fruits, certain vegetables containing abundant cellulose, and berries containing small seeds may, in some individuals, readily provoke an attack of diarrhœa that can be explained by the mechanical irritation occasioned by the unabsorbable residue. Other foods, such as fish, shell-fish, cheese, milk, etc., may easily undergo decomposition in the bowels or may contain preformed products of decomposition, particularly in hot weather, and thus may excite more or less acute or violent diarrhœa. Various microorganisms have been found in association with cases of this sort. Mere excess of food may set up a diarrhœa as a result of derangement of the gastric and upper intestinal digestion and secondary bacterial fermentation.

**Diarrhœas Due to Purgative Substances.**—Any of the various purgatives used in practical medicine may occasion active diarrhœa. The majority of these act upon the muscle of the bowel and its nervous mechanism without influencing the secretions or absorptive processes. Their effect is simply to stimulate peristalsis, especially that of the large intestine, and thus to hasten the contents of the bowel through the tract. The salines increase watery secretion from the intestinal mucous membrane; and some exercise a stimulating effect upon peristalsis.

**Diarrhœa Due to Nervous Influences.**—A variety of conditions may excite increased peristalsis by directly affecting the nervous mechanism of the bowels. The influence of shocks, fright, fear, and various kinds of excitement, is well known. In some diseases attended with disorders of the nervous system, like Graves' disease, hysteria, or neurasthenia, attacks of diarrhœa or continued looseness of the bowels may occur. In some persons the nervous mechanism of the intestines appears particularly susceptible, and slight influences, such as emotional conditions, exposure to cold, or various forms of irritation ordinarily having little effect, may readily increase peristalsis. The condition known as morning diarrhœa, in which several evacuations occur in the early morning, after which the bowels remain quiet until the next day, may be explained by assuming the existence of an irritable state of the nervous mechanism in the lower bowel, and the consequent prompt evacuation of contents that usually reach this portion of the tract twenty-four hours after the beginning of ingestion.

**Diarrhœa Due to Diseases of Other Organs and Disordered Conditions of the Blood.**—In some cases of heart disease, congested conditions of the mucous membrane of the bowel may occasion a proneness to diarrhœa, or may cause it directly by increasing intestinal secretion. The association of diarrhœa with renal disease is more important than either of the others. In this case the vicarious excretion of urea from the intestinal mucous membrane and the decomposition of this, with the production of ammonium, occasion irritation, sometimes of intense character. In



all cases of severe kidney disease the development of diarrhoea must be regarded with suspicion.

More or less intense diarrhoea may be associated with various infections not necessarily involving the intestinal tract itself. Thus, in cases of septicopyemia and pneumonia, and in various other infections with lesions at a distance from the bowel, diarrhoea may occur. There is reason to believe that such attacks are due to the elimination of toxic matters from the intestinal mucous membrane, just as urea is eliminated in cases of disease of the kidneys. Recent experiments have shown that the toxins of such organisms as the *Bacillus dysenteriae* injected hypodermically may be eliminated through the bowel, causing secondary lesions of the mucous membrane. The same is true of injections of cholera toxin. Even in infections of the intestinal tract, therefore, such as cholera, dysentery, etc., the attending diarrhoea may be due to the toxic state of the blood and the secondary elimination of the toxins through the mucous membrane of the bowel.

**Diarrhoea of Gastric Origin.**—In certain diseases of the stomach, especially in achylia gastrica, a tendency to diarrhoea may sometimes be a marked feature of the clinical history. In achylia this has been attributed by some to the absence of free hydrochloric acid and consequent failure of the normal anti-bacterial action of the gastric juice, while others believe it results from the lack of sufficient stimulus for efficient pancreatic secretion and consequent failure of digestion. The offensive character of the stools and the presence of large numbers of bacteria lend some color to the former view, while the amount of undigested food residue, especially meat fibres, supports the other view.

Diarrhoea may also occur in cases of marked hyperacidity of the stomach, though in this case it is usually only a temporary occurrence in persons usually constipated.

**Diarrhoea Due to Intestinal Indigestion.**—Certain persons are liable to attacks of fermentative diarrhoea apparently of intestinal origin and particularly after taking some particular kind or kinds of food. The gastric conditions are found to be normal, but distension, colicky pains and the passage of fermenting, highly offensive and acid stools of a crumbly character occur during the attacks. At times this condition is quite obstinate. The stools are often light from admixture of gases of fermentation and float in water; they may be light yellowish or brownish in color and contain abundant microorganisms of fermentation.

**Diarrhoea Due to Organic Diseases of the Bowel.**—In connection with enterocolitis and other catarrhal and inflammatory conditions of the mucous membrane, in the descriptions of the various ulcerations of the bowels and of malignant disease, diarrhoea will be discussed.

**Bacteriology of Diarrhoea.**—Bacteria and their products are sometimes the direct causes of diarrhoeal conditions. A considerable variety of microorganisms may be concerned and it is difficult to determine with certainty in many cases which of the abundant intestinal flora is mainly operative. Certain facts have been learned by observations of the predominant organisms in different cases, by the discovery of forms in

abundance that normally are not present and that have been traceable to tainted food, and by the application of agglutination tests to the serum of individuals suffering with diarrhoea.

Certain of the normal organisms of the intestines to which the system has grown accustomed may under peculiar circumstances undergo unusual multiplication or increase of virulence, so that they become pathogenic. Among these the *Bacillus coli communis* is most important. The fact that this organism is largely present in cases of diarrhoea does not necessarily imply its etiological relation, although other considerations may establish it. There is little doubt that under some conditions diarrhoeal diseases are caused by this group of organisms.

Closely allied organisms, such as the *Bacillus enteritidis* of Gaertner, and members of the intermediate group, the paratyphoid and paracolon bacillus, are important causes of certain diarrhoeal conditions. Diarrhoea due to the *Bacillus enteritidis* has been found in some cases of meat poisoning and sometimes also in cases not directly traceable to the consumption of tainted meat. In some cases, especially in the diarrhoeas of childhood, streptococci and staphylococci appear to be the active agents and may cause intense forms of enteritis. Among less frequent causes are various others of the organisms named as inhabiting the intestinal tract normally which may operate by their direct action or by causing fermentative processes with the liberation of fatty acids and other irritant substances that secondarily occasion intestinal disturbance and diarrhoea. In the disorders of intestinal fermentation organisms of fermentation may be conspicuous—among these the clostridium butyricum or granulobacillus, saccharobutyricus, and long bacilli (Oppler-Boas?), *Bacillus pyocyaneus*, Friedländer's bacillus, the *Bacillus botulinus*, and other forms occur more rarely. Certain organisms of specific diseases, such as typhoid fever, tuberculosis, syphilis, etc., occasion characteristic lesions and often an associated diarrhoea.

Diarrhoea is sometimes occasioned by protozoa, including amœbæ and a variety of flagellate and ciliated forms.

**Symptoms.**—The clinical manifestations of diarrhoea depend largely upon the nature of the condition and the part of the bowel involved. In cases of irritation of the *upper* intestine due to overloading with food or functional derangement, diarrhoea may not occur if the peristalsis of the colon remains normal; but usually an increase of activity occurs in this part of the tract as well, and some looseness results. In such cases the stools are likely to present features that indicate that the upper bowel is at fault. Undigested food, with the admixture of considerable mucus, rendering the feces pasty, sticky, or viscid, and a yellowish or greenish coloration, due, in part, to unaltered bile and largely, often, to pigment derived from bacterial action, are characteristic. Excessive acidity may render the discharges highly irritating, and may occasion secondary inflammatory conditions of the rectum, anus, or even of the skin externally. This is commonly met with in diarrhoeas of this type in childhood.

In cases of widespread irritation of the bowels, involving both the large and the small intestine, more copious watery discharges are the

rule. There is usually an admixture of fecal matter, and the color of the movements may vary from a dark brown to a light yellow; or, when abundant serous outpourings occur, as in choleric forms, almost watery discharges are seen.

When the *large* intestine is particularly involved there is usually considerable mucus of whitish color, and more frequently in masses than in cases involving only the upper intestine. It may be seen as jelly-like particles or as large accumulations; and sometimes, alternating with the discharges of ordinary diarrhoeal type, the evacuation of almost pure mucus or mucus streaked with blood may be encountered.

The subjective symptoms in cases of moderate diarrhoea may be very slight. As a rule, however, when the small intestines are involved, colicky pains and abdominal tenderness are usual. In some instances this may be intense, and the patient may become prostrated from the severity of the pain, as well as from the loss of water and other causes. In cases of diarrhoea involving special irritation of the lower bowel, local tenderness in the left flank or above the pubis may signify involvement of the descending colon and sigmoid. In these cases, also, tenesmus is not unusual.

Soon after the onset of diarrhoea a certain degree of weakness or prostration is usual. In mild cases this is of little consequence. In severe forms extreme prostration or collapse may occur. The circulation becomes enfeebled; a little cyanosis may be present; and in children, sinking of the eyes and fontanelles, pinched features, and other indications of the Hippocratic facies are seen.

Fever is rarely found in mild cases, but slight elevations are not unusual in the more severe. On the other hand, the prostration may be such that the temperature soon becomes subnormal.

Disturbance of the stomach sometimes attends diarrhoea, either as a result of the original dietary disturbance or other irritation that has occasioned the diarrhoea, or as a reflex result of pain and irritation.

The clinical *course* of cases of diarrhoea varies with their cause and nature. In ordinary instances due to digestive disturbance a few evacuations succeeding each other at intervals of a half hour to several hours may terminate the condition. In more severe cases, and particularly when more intense irritation of the intestines has occurred, the diarrhoea may increase in severity for a day or two, or may reach its maximum only after several days. In such instances the stools tend to become more and more watery as the contents of the bowel are evacuated, while in cases in which the large bowel is involved there may be, in the later stages, only discharges of mucus. In most instances the entire duration is not above several days, unless secondary enteritis or colitis has complicated the condition.

**Diagnosis.**—This is mainly concerned with the recognition of the cause. Ordinary diarrhoea must be distinguished from various forms of specific intestinal disease or general infections accompanied with intestinal manifestations.

**Treatment.**—Prophylaxis is of great importance. The avoidance of irritating or tainted foods, particularly during hot seasons of the year



when decomposition is apt to occur, is the most important measure. Uncooked fruit, shell-fish of various sorts, berries, and cold drinks are among the articles of diet to be scrutinized with greatest care. Residents of hot climates have found it advantageous to wear an abdominal band of flannel or some woven material, to secure warmth and protection, particularly when cool nights succeed hot days. Local applications of heat over the abdomen, in the form of hot-water bags, hot fomentations, and binders of various sorts, are often quieting in the onset and may moderate the severity of the attack by controlling peristalsis.

**Diet.**—The diet during an attack of diarrhoea should be extremely moderate in the beginning, and often it is necessary to avoid food altogether. Later, and particularly in cases in which prompt control is not secured, a cautious increase of food is requisite, lest the patient's strength be too greatly impaired. Thirst, which may be complained of severely, should be controlled by the swallowing or eating of small bits of ice and the sipping of small amounts of cold water. Frequently, merely holding water in the mouth is satisfying. Albumin-water, barley-water, rice-water, or toast-water may be used to quench thirst and, at the same time, to supply a certain amount of nourishment. If the stomach is irritable, these liquids may be better tolerated than plain water. After preliminary evacuation of the bowels has been secured, a diet of pasteurized or boiled milk, given in small quantities, or milk with well-cooked farinaceous foods, such as arrow-root, rice boiled in milk, milk toast, etc., may be given. Later soft-boiled eggs, gelatin preparations, such as meat jellies, and, still later, scraped beef or minced chicken, may be allowed. It is usually advisable to avoid giving vegetables until the signs of gastro-intestinal irritation have subsided.

**Medicinal Treatment.**—After the onset, the first consideration in the treatment is the evacuation of irritating material, if the spontaneous discharges are not enough to carry these off. Nearly always it is desirable to use some unirritating and rapidly acting purge, such as castor oil. It is a common practice to add to this a small amount of tincture of opium or paregoric, to allay irritation and prevent unnecessary griping. Other purgatives, such as calomel, salines, magnesia, and the like, may be used instead of castor oil; but they are less prompt in their effects. After evacuation of the irritants the use of sedatives is desirable. Bismuth powders, to which may be added pepsin, if digestive disturbances are present, chalk mixture, cerium oxalate, lime-water, or other alkalis may be used to quiet intestinal irritation and neutralize acidity. A combination of chalk mixture with paregoric and some astringent, like tincture of kino or catechu, is frequently used.

When cramp-like or colicky pains are present, some form of sedative and carminative may be added or substituted for the remedies named. Chlorodyne or improvised mixtures containing other carminatives, such as spirit of chloroform, compound tincture of cardamom, or spirit of ginger, with opium, may be employed for this purpose. When intense pains occur and collapse threatens, the timely use of a hypodermic injection of morphine, followed by the various remedies already named, may cut short an attack that promises to be serious. Sometimes sup-

positories of opium may be substituted for these, or repeated doses of paregoric or of tincture of opium may be given by the mouth.

Sudden diarrhœas, attended with marked evidences of intestinal irritation, should be treated with promptness; and active remedies, astringent, sedative, and protective, should be given early. As a rule, the evacuations are so free that little is gained from a preliminary administration of purgatives; and these may, at times, be actually harmful. Bismuth in fairly large doses (gr. xxx, gm. 2), in the form of the subnitrate, subgallate, or salicylate, with vegetable astringents, such as kino or catechu, repeated doses of opium, and an occasional hypodermic of morphine, may be given. Mineral astringents sometimes have a greater controlling effect than the vegetable forms. Small doses of subacetate of lead or nitrate of silver may be employed.

When diarrhœa becomes obstinate or chronic, persistence in the use of the same kind of treatment, using small doses of the various drugs named, will gradually control the disorder. Diet here, however, plays a more important rôle than does the medicinal treatment. No general rules can be laid down regarding the most desirable diet, as individual peculiarities play an important part and therefore require individual consideration. In most cases the use of pasteurized or boiled milk, with or without small amounts of farinaceous food, proves most suitable. In some persons, however, milk is not tolerated; and even forms of food prepared with milk may protract the diarrhœa. In such individuals, eggs and rare meat, with a farinaceous diet, may prove more acceptable. Occasionally the use of some astringent water, like the Rockbridge alum water, aids in controlling a persistent diarrhœa.

*Nervous diarrhœas* are best treated with remedies directed to the general nervous system and careful regulation of the diet, so that any undue taxing of the digestive functions may be obviated.

Diarrhœa attended with irritation of the lower bowel sometimes requires local treatment. In the acute stages, if tenesmus, pain, and other local symptoms are marked, relief may be obtained from ice suppositories or from the injection of small quantities of cold water or larger amounts of starch water containing tincture of opium. When a residual catarrhal condition persists, the cautious use of colonic injections of weak solutions of nitrate of silver (1 to 5000) may be useful; but repeated injection and stronger solutions may easily do harm.

### ACUTE ENTERITIS

**Definition.**—This term may be employed to designate acute catarrhal inflammation of the mucous membrane of the small intestine as well as the upper portion of the large bowel. The terms acute inflammatory diarrhœa, enterocolitis, and ileocolitis are synonymous with that here preferred. It is impossible to distinguish this condition sharply from irritative diarrhœas due to digestive disturbances and certain infectious diseases with intestinal manifestations. In the former group are cases in which actual enteritis results from the highly irritating character of products of intestinal fermentation. In the latter group are many

infections often situated at a distance from the intestinal tract, in which complicating enteritis results from irritating toxins in the blood, excreted into the bowel. There must also be remembered the specific infectious diseases, such as typhoid fever, cholera, dysentery, etc., in which enteritis is an important lesion.

**Etiology.**—Individual susceptibility often plays a part, certain persons being exceedingly liable to this form of disease. Enteritis is more common in hot weather and in hot climates than at other times or elsewhere, owing to the greater likelihood of the contamination of food in these circumstances, and because certain easily tainted foods like fruit are more commonly used. As in childhood, chilling of the surface during cool nights following hot days plays some part in the etiology.

The direct cause is usually some chemical irritant contained in food. The irritants, however, may reach the intestines through the circulation. They are quite varied, depending upon the character of the food, its preparation, and its preservation. Sometimes, although wholesome when swallowed, excessive quantities of food or digestive disturbances may occasion fermentation in the intestinal tract and the formation of irritants that directly excite a catarrhal inflammation. *Bacteria* probably rarely cause catarrhal inflammation directly. Usually their relation is that of agents causing fermentative changes in food or intestinal contents, and the products of such fermentation are the immediate causes of the resulting enteritis.

Among other causes of enteritis must be named mineral poisoning, or poisoning by toadstools or other noxious substances. Overdoses of lead, mercury, arsenic, copper, and other mineral substances may occasion intense forms of enteritis with violent symptoms.

**Pathology.**—The mucous membrane of the bowel may be involved with almost equal severity from the stomach to the upper portion of the large intestine, but usually certain areas are more seriously implicated than others. The mucosa is swollen and reddened. Often the crests of the valvulae conniventes alone present an inflammatory appearance. The surface is usually covered with mucus, which may be blood-tinged, and sometimes hemorrhagic extravasations occur in the mucosa. The lymphatic follicles are swollen and stand out prominently as light areas against the inflamed surface. The Peyer's patches may be swollen, and occasionally show small rounded ulcerations.

In exceptionally violent forms, pseudomembranous or diphtheritic inflammation of the mucous membrane of the small and large intestine may occur. Sometimes this is primary, in the sense that no preceding infective lesion can be discovered; but much more commonly it is secondary to infections originating elsewhere. The same form may be met with in cases of chronic nephritis or uremia, following cirrhosis of the liver and other conditions producing portal obstruction, and in association with obstructions of the bowel caused by carcinoma or other lesions. Sometimes an intense enteritis with pseudomembrane formation occurs as the result of mineral poisoning, such as is caused by mercury.

**Symptoms.**—The clinical manifestations vary with the intensity of the cause and the part of the intestinal tract principally affected. In



milder cases the symptoms are those of ordinary diarrhoea due to dietetic errors and functional disturbances. In severe cases the manifestations are sudden and violent.

The *stools*, as a rule, are of ordinary diarrhœic character, liquid, brownish, and more or less offensive, according to the degree of putrefactive change taking place. In the beginning there may be merely pultaceous movements which evacuate the lower bowel; later the movements become more watery, and frequently contain a certain amount of visible mucus. When the large intestine is especially affected, the amount of mucus may become considerable; but in most cases the discharges remain thin, watery, and brownish. When enteritis is due to irritants of great intensity, very frequent and abundant watery movements result; and an excessive diarrhoea, approaching in severity that of an attack of true Asiatic cholera, may occur. Sometimes constipation instead of diarrhoea is met with in cases of enteritis, the explanation of this being that inhibition instead of stimulation of peristalsis has resulted from the irritation. Undoubtedly many cases of acute constipation following indiscretions in diet and irritation of the upper part of the small intestine are produced in this manner. When actual enteritis is present, and especially when it is extensive, diarrhoea practically always results. In some cases of intense and localized enteritis paresis of the affected segment of bowel may occasion intense constipation or even complete obstruction of the bowel.

The patient usually suffers with colicky pains and more or less abdominal soreness from the beginning. As a rule, this is of moderate severity, but sometimes it becomes extreme. Distension of the abdomen from gaseous accumulations may occur, and loud rumbling or gurgling sounds (*borborygmi*) are frequently heard. In some cases, owing to great severity of inflammation in a certain restricted part of the bowel, intense pain and tenderness may be found in a localized area of the abdomen. When the lower part of the ileum is involved the local symptoms may suggest appendicitis. In these cases rigidity of the abdominal muscles in the area of pain and tenderness, the occurrence of fever, of vomiting, and of leukocytosis may still further confuse diagnosis. The development of diarrhoea is usually the determining symptom in the establishment of a proper diagnosis, but this may be wanting in enteritis, and in exceptional cases is met with in appendicitis.

In the beginning, irritation of the stomach is usually met with, and vomiting may be a disturbing symptom at the onset. Later, this subsides, as the intestinal symptoms become more pronounced. Some gastric disturbance, however, usually persists. The tongue becomes coated and dry, appetite is wanting, there is more or less nausea or distress after eating, and frequently vomiting is easily provoked throughout the course. When the upper part of the small bowel is especially involved, active gastric symptoms may be a conspicuous feature of the clinical manifestations. Continuous nausea and vomiting and localized pain in the upper part of the abdomen are marked. Sometimes moderate jaundice indicates a special involvement of the duodenum.

*Fever* is more or less high from the beginning, some elevation of temperature rarely being absent. The temperature bears no relation to the severity of the intestinal manifestation. In extensive enteritis of moderate severity a continuous febrile temperature resembling that of typhoid fever may occur, and the diagnosis is therefore at times quite uncertain.

The patient suffers with loss of strength and general debility, in proportion to the degree of irritation and the intensity of the diarrhœa. In cases in which large, watery evacuations are frequently repeated the patient may fall into a state of rapid prostration or collapse. In such instances the surface becomes cold and moist, cyanosis of the extremities may be noted, or there may be complete collapse.

The physical signs, as a rule, indicate nothing beyond a slight abdominal distension, with more or less tenderness on pressure. In some cases, however, marked tympany is observed.

The secretions become scanty, the urine particularly being reduced in quantity, and often presenting a certain amount of albumin with hyaline or granular casts. In intensely infective cases, acute nephritis may occur. Examination of the blood reveals moderate grades of leukocytosis.

In cases of diphtheritic enteritis secondary to infective lesions elsewhere, high fever, intense intestinal symptoms, and rapid prostration of strength are usually encountered. The evacuations in these cases may contain shreds of pseudomembrane or of exfoliated mucosa, and sometimes blood and pus.

**Cholera Nostras.**—Cholera nostras, or cholera morbus, is an intense form of acute enteritis, bearing the same relation to ordinary cases of enteritis of adults as cholera infantum bears to ordinary enterocolitis in childhood.

**Etiology.**—This occurs with greatest frequency in the summer months, and is usually, although not always, traceable to some error in diet. Probably in many cases bacterial infection plays an important part, although no particular form of organism is associated with it. In some cases, preformed products of bacterial decomposition in the food are active; in other cases it is probable that, as the result of digestive disturbance after errors in diet, bacterial decomposition takes place in the stomach or intestinal tract. Chilling is an important etiological factor. Exposure during cool nights following hot days, and when the surface has been relaxed and moistened by active perspiration, is particularly important.

The pathological anatomy does not differ essentially from that of other forms of enteritis. There is, however, a tendency to marked exfoliation of the mucous membrane and follicular infiltration; and, as the consequence of intense serous outpourings, desiccation and anemia of various organs may be discovered.

**Symptoms.**—The onset is sudden and violent, usually beginning with nausea and intense vomiting and violent abdominal pain. The patient speedily falls into a condition of prostration from the intensity of the suffering and the violent nausea and vomiting. The contents of the stomach are soon evacuated, after which bilious vomiting takes

place; and finally, watery liquid is discharged, or intense unproductive retching may ensue. Soon after the onset diarrhœa begins. After the discharge of the contents of the lower bowel the movements become copious, watery, and frequently repeated. They are discharged without special effort or tenesmus, and may finally become almost or quite involuntary. From beginning to end the tendency to large, watery evacuations is a marked feature.

The abdomen is tender, and sometimes excessively so. The patient in the beginning lies upon the side, with the legs flexed to relieve pressure, or upon the back, with the thighs flexed upon the body. Later, sensation becomes less acute, owing to prostration, and pain and tenderness become less marked. At the onset the temperature rises, and sometimes reaches a considerable degree of elevation. Exceptionally, hyperpyrexia may occur. Later, as prostration increases, the surface temperature falls; and finally the extremities, the face, or the whole body may become cold. The rectal temperature, however, may remain elevated to the end. The secretions, and especially the urine, become scanty. Albumin and casts are generally present.

In severe cases the patient falls into a condition of collapse, hardly distinguishable from that of true Asiatic cholera. The face is cold and cyanosed, the lips dry, the tongue parched, the breath cold, respirations feeble, the voice suppressed, the pulse weak and thready, and the general condition is one of intense prostration, stupor, or collapse. In mild cases, after a sudden onset and somewhat intense symptoms, the diarrhœic discharges become less severe, the vomiting ceases, fever subsides, and a gradual amelioration of other symptoms occurs. After a day or two practical recovery may ensue. In severe cases the symptoms continue unabated or increase in severity, and finally collapse occurs.

**Diagnosis.**—The recognition of enteritis offers no great difficulty in most cases. The history, onset, abdominal pain, and diarrhœa are characteristic. When the large bowel is considerably involved it may be difficult to determine whether the enteritis is one of ordinary type or dysenteric. Bacteriological examination of the stools and serum reactions may in these cases be required to establish a correct diagnosis. Sometimes enteritis presents a puzzling resemblance to typhoid fever. The suggestive features in these cases are continued fever, diarrhœa, general prostration, loss of appetite, coated tongue, and headache. The occurrence of splenic enlargement, rose spots, and the characteristic serum reaction eventually establishes the diagnosis in typhoid fever, but a week usually elapses before these occur. Before that time leukocytosis, negative blood culture, general abdominal soreness, and the urgency of the diarrhœa may aid in excluding typhoid fever.

There may be difficulty in distinguishing some cases of enteritis from appendicitis. As a rule, the correct interpretation will be made possible by the persistence and increase of the local signs (tenderness, rigidity, tumor), by the occurrence of repeated nausea and vomiting and perhaps chills, and by increasing leukocytosis. Obstinate constipation, while not necessarily diagnostic, is strongly suggestive of appendicitis.

The diagnosis of cholera nostras usually offers no difficulty whatever.



In times of epidemics of Asiatic cholera, however, cases occur in which the diagnosis cannot be made. Under these circumstances no safe rule can be adopted other than to regard all choleraic diarrhœas as of the specific type, particularly as it is well known that mild cases of true Asiatic cholera are frequently seen in epidemics of that disease.

**Prognosis.**—This is favorable in cases of ordinary enteritis in adults. Unless the cause is one of unusual severity, recovery usually takes place. In the old or enfeebled, however, as in children, the disease is one of considerable gravity. Usually after a few days of urgent symptoms, gradual amelioration takes place, terminating in complete recovery. Sometimes the condition ends in a subacute, or even a chronic disease.

**Treatment.**—Prophylactic treatment is of the first importance. Among important preventive measures are the avoidance of irritants, tainted food, and the like, especially in hot seasons; in institutions in which numbers of persons are closely associated, or in camps, barracks, and the like, the closest scrutiny of the food and water supply during the hot seasons of the year is necessary. Careful attention to the dress, especially the wearing of abdominal bands, is of importance in susceptible individuals and is a useful precaution.

The treatment of *acute enteritis* is practically the same as that of ordinary diarrhœa, and therefore needs no extended discussion. The patient should be kept strictly at rest. The temptation to remain out of bed occurs only in mild cases, as the symptoms in severe forms are usually marked enough to make the patient take to bed at once. In the beginning of mild cases, however, matters may be made more serious by any attempt to continue at ordinary occupations, and in severe cases premature release from the bed may cause recurrences. The diet should be restricted to liquids, such as boiled milk, broths, gruels, albumin-water, and the like, or should be interdicted entirely. When vomiting or gastric symptoms are present, it is, as a rule, advisable to withhold all food in the beginning.

Warm applications, such as fomentations, hot-water bags, poultices, or the like, not only give great comfort but have a controlling effect on peristalsis, and thus aid in checking diarrhœa. When distension of the abdomen is troublesome, turpentine stupes may be advantageous.

As soon as the nature of the disease is recognized, the first care must be the removal of irritants from the intestinal tract. Unless diarrhœa is active from the first, a full dose of castor oil or some saline may be used to evacuate the contents of the bowel. If the symptoms in the beginning are not urgent, calomel followed by a saline may be employed. After copious evacuation has been secured, measures should be taken to control the diarrhœa and the intestinal inflammation. Bismuth salts, chalk mixture, lime-water, and other alkalis are advisable when acid fermentation is active. Astringents, such as kino, catechu, or various other tannic acid preparations, may be used. The addition of opium in the form of Dover's powder, laudanum, or paregoric is advisable when diarrhœa is severe and pain is marked. A timely injection of morphine in the beginning may control the severity of the attack. In later stages, when the diarrhœa has become less urgent and the general

symptoms are less pronounced, such astringents as silver nitrate or acetate of lead may be used in combination with opium.

In *cholera morbus* the prompt use of opium by mouth or rectum, or of hypodermics of morphine, is advisable. The intensity of the vomiting usually precludes the administration of remedies by the mouth until the condition has been somewhat controlled. After this result has been secured, the treatment may be conducted as in ordinary cases. When symptoms of collapse appear, hot applications over the abdomen are advisable; hot drinks, with the addition of small doses of brandy or other stimulants, may be given; and hypodermic injections of strychnine, camphorated oil, tincture of digitalis or digitaline, etc., should be employed. When the symptoms have somewhat subsided, great care should be exercised in resuming ordinary diet. Small quantities of liquid food alone should be permitted, and these should be given at short intervals and cautiously increased. If a tendency to nausea persists, cerium oxalate with fractional doses of cocaine or codeia may be administered before food, so that the stomach may be less irritable.

### CHRONIC ENTERITIS

This is a condition of catarrhal inflammation of the small intestine and the upper part of the large intestine, with or without ulceration. It usually follows as the sequel of acute attacks.

**Etiology.**—This disease may result from a severe attack of acute enteritis or may be caused by repeated slight attacks. Not infrequently it is an accompaniment of other conditions of the bowel, as carcinoma, intestinal obstruction, etc. Certain individuals show a distinct tendency to repeated or chronic catarrh of the bowel.

**Pathology.**—The intestines usually present evidences of long-continued inflammation of the mucous membrane. The surface is covered with excessive secretion (mucous or mucopurulent), and there are areas of thickening of the mucosa or of erosion and atrophy. Ulcerations and stellate cicatrices of healed ulcers may be found, especially in the large bowel. Sometimes polypoid formations are found surrounding ulcers or independent of any ulceration. The mucosa may be of a normal color or hyperemic and more or less pigmented.

**Symptoms.**—The conspicuous symptom is persistent or intermittent *diarrhœa*. The movements are extremely variable in character, sometimes being nearly normal, at other times soft and pultaceous, or foamy, from the occurrence of fermentative processes. In still other cases they are large and liquid, and their color varies from a light yellow to a dark brown. Frequently they become highly offensive during exacerbations, when increased bacterial putrefaction occurs. In some cases, instead of diarrhœa there is persistent *constipation*. In these cases light-colored or gray scybalous masses, more or less coated with mucus, may be passed; while at intervals attacks of diarrhœa, with soft or liquid movements, occur. When the large intestine is specially involved, mucus is always a pronounced feature in the movements, and at times

masses of mucus may be passed without any fecal matter. Blood-streaked movements or decided losses of blood may occur in cases attended with ulcerations or polypoid conditions of the mucosa.

The abdomen is usually distended when chronic enteritis affects a large part of the intestinal tract. In cases in which the process has become limited to a restricted area, distension may be wanting, and local discomfort or tenderness alone may be discovered.

The general state varies greatly. In many individuals this condition persists for years without great impairment of the health. In others, emaciation, general depression, and a variety of nervous symptoms significant of a lowered vitality are met with. Hypochondriac and neurasthenic symptoms are not unusual, as in cases of mucous colitis. The patient may become extremely emaciated, anemic, and weakened, and not rarely sinks into a state of semi-invalidism. The highest grades of anemia are observed in cases in which ulceration causes loss of blood or in those in which bacterial putrefaction occurs actively.

**Diagnosis.**—It is difficult to distinguish chronic enteritis from functional disturbances of the intestine on the one hand, and from mucous colitis or certain primary nervous disorders on the other. In enteritis affecting the upper bowel the stools are found to contain undigested food, and are often acid in reaction, as in cases of intestinal indigestion. The intensity of the symptoms and the associated indications of inflammatory trouble alone make a distinction possible. No absolute line of division can be drawn between the two conditions. When the large intestine is specially involved and mucus is abundant in the stools, chronic enteritis closely resembles mucous colitis. The latter, however, is usually so closely associated with primary conditions of nervous debility, and the evidences of intestinal irritation are so inconspicuous as compared with those in enteritis, that a distinction is usually easily made. The history of onset is also of importance in the diagnosis.

Many individuals suffering with nervous diseases, such as neurasthenia, are liable to attacks of diarrhœa, or may suffer with more or less continued looseness of the bowels, which may suggest an intestinal origin for the nervous condition. In these cases, however, acute symptoms of irritation of the bowels are generally wanting and the manifestations are those of intestinal indigestion, rather than of enteritis. When a chronic form of enteritis occurs in tuberculous or syphilitic persons it may be difficult to determine whether it is a simple enteritis or one of specific character. The clinical course and the results of treatment must determine.

**Prognosis.**—Chronic enteritis may continue for weeks, months, or years. The prognosis is always uncertain but persistent treatment is generally helpful, though not always completely effective.

**Treatment.**—The removal of all sources of irritation is the first care; sometimes an established error of diet may be discovered and corrected. In other cases a modification of the habits of life and the avoidance of exposure, fatigue, and similar causes are important. A close supervision of the patient's diet and an individual study may discover idiosyncrasies. Sometimes the correction of gastric digestion and the use of remedies



such as nux vomica or other stomachics and digestive ferments may relieve the condition. Usually, however, some form of astringent medication is indicated. Of all remedies of this class nitrate of silver is the most important. This may be combined with extract of opium or extract of nux vomica and administered in the form of pills coated with salol or keratin, which secure the passage of the pill through the stomach and its solution in the alkaline secretions of the intestine. Other astringents such as acetate of lead and bismuth salts may be employed. All the remedies are best given in small doses frequently repeated. When fermentative processes are active, guaiacol carbonate or salol may be employed in small doses, as such remedies, by irritating the mucous membrane, may increase rather than decrease bacterial proliferation.

In cases involving the large intestine local treatment is advisable, such as repeated irrigations of the colon with water or saline solution. When mucus formation is abundant, astringent injections, as solutions of nitrate of silver (1 to 5000), quinine (1 to 5000), or the addition of fluid extract of hamamelis to a saline solution (1 to 125), may be employed.

### COLITIS

Inflammation of the colon frequently occurs as an accompaniment of general catarrhal inflammation of the bowels or enteritis and is a common accompaniment of organic diseases of the large bowel. It is also met with as a manifestation of certain specific infections, such as dysentery. Occasionally, however, colitis occurs as an independent disease. This form alone is now under consideration. The term *simple colitis* has been applied to such cases by Hale White.

**Etiology.**—The causes are similar to those of enteritis, and no adequate explanation can be given for the limitation of the disease to the large bowel. Some cases seem to follow the dislodgment of hardened masses of fecal matter from the sigmoid flexure. Doubtless the retention of scybala in the pouches of the large bowel is quite sufficient to cause inflammation. Dietary errors and various irritants doubtless play a part, and often infections are concerned. No specific microorganism, however, is operative in these cases. Colitis sometimes occurs as a secondary manifestation in certain general infectious diseases, such as pneumonia, septicopyemia, etc., and also in nephritis and uremia.

**Pathology.**—The mucous membrane of the bowel presents the usual appearances of inflammation with thickening of the mucosa, excessive mucus formation, and follicular ulceration. In persistent cases polypoid formations may be met with, and pigmentation or hemorrhagic extravasation may be seen. In the colitis attending violent infections pseudo-membranes are sometimes observed.

**Symptoms.**—The principal manifestations are diarrhœa, local pain, and tenderness. The stools contain an abundance of mucus, and are often blood-tinged. Sometimes considerable hemorrhage may occur. In severe cases, small mucous, blood-tinged discharges, resembling those

of simple dysentery, occur and may be frequently repeated. In subacute cases fecal matter, with mucus and blood, is passed. Abdominal pain, especially in the region of the sigmoid flexure, is usually complained of, and sometimes there is extreme tenderness on pressure. This may be so great that the patient lies with the left thigh flexed; and even the weight of the bedclothes may be intolerable. The pain is increased at the time of the movements, and active tenesmus may occur.

Fever and general prostration of more or less intensity are usually present, and gastric disturbances may occur, although these are not, as a rule, severe. In old and debilitated persons extreme prostration frequently presents itself. In the pseudomembranous colitis accompanying infections a rapid loss of strength, high fever, and prostration result.

**Diagnosis.**—The acute onset, local tenderness, and mucous discharges are the most characteristic features. It is extremely difficult to distinguish a simple colitis from dysentery or from enterocolitis with special involvement of the large bowel. It must be remembered that colitis occurs as a symptom of malignant disease and other organic conditions.

**Prognosis.**—This is usually favorable, although a tendency to chronic inflammation sometimes results. In persons weakened by age or previous disease a fatal termination may occur.

**Treatment.**—Rest and warm applications to the abdomen, with careful regulation of the diet and the administration of remedies to check intestinal irritation, are the important features. All of these have been considered in the discussion of the treatment of diarrhœa and enteritis. Special mention may, however, be made here of certain local methods of treatment. When the inflammation in the sigmoid flexure and rectum is pronounced, and tenesmus is a troublesome symptom, ice suppositories, injections of small quantities of cold water, or of starch-water containing opium, cocaine, or other sedatives, may be used with advantage. Cases marked by more extensive irritation, or in which hard scybala tend to form, are benefited by repeated injections of small quantities of olive oil. In subacute cases and during the later stages of acute attacks astringents of various sorts may be used in larger colonic irrigations.

## DIARRHŒA IN CHILDHOOD

The diarrhœas of infancy and early childhood require special consideration, on account of their greater urgency and their distinctive features. As the digestive and metabolic functions are relatively predominant at this age, any derangement of the gastro-intestinal tract naturally involves a greater disturbance of health.

**Etiology.**—The causes of diarrhœa in children are practically the same as those in adults, but the difference in the character of the food, in the routine of life, and in susceptibility give a greater prominence to certain conditions.

**Food.**—Probably the most generally active cause of diarrhœa in children is improper feeding. A mere excess of food may be sufficient to derange digestion and occasion intestinal irritation; but overfeeding

is particularly harmful because it furnishes favorable conditions for bacterial growth and fermentative processes in the intestinal tract. This is particularly seen in young children past the nursing age, in whom a single overloading of the stomach may occasion an attack of diarrhœa, afterward prolonged by secondary conditions. The more indigestible the food the more promptly will diarrhœa follow and the more serious its type. In sturdy, bottle-fed infants an appetite somewhat too keen may readily tempt the mother or nurse to overfeed the child, and diarrhœa frequently results. The quality of food, especially milk, must be considered. Diarrhœa in young infants is frequently caused by milk containing too high a percentage of fat.

Much more commonly the cause is some qualitative changes in the food, especially the use of tainted milk. Attempts to improve conditions by pasteurization or sterilization of the milk are of questionable utility, although the former plain is preferable. Sterilized milk should be condemned, because its constant or repeated use undoubtedly occasions nutritional disturbances, infantile scurvy, and other diseases. Pasteurization, although less objectionable, cannot be relied upon to destroy all micro-organisms, and thus often gives a false sense of security. Experimental investigations have shown that after thorough pasteurization bacterial multiplication occurs even more rapidly than in raw milk; and when the food is prepared in the morning, the bottles given later in the day may be in worse condition than if pasteurization had not been practised. The addition of any bactericidal agent to milk, even in minimal quantities, must be unreservedly condemned. Intense forms of diarrhœa and general infection are sometimes followed by the use of milk obtained from cows suffering with mastitis.

Safety in milk feeding lies in the careful supervision of dairies, the handling of the milk in the cleanest possible manner, prompt delivery at the home, and careful refrigeration after its delivery.

Sometimes, although the milk used has been fresh and pure, diarrhœa may follow its use on account of disturbance of digestion and secondary fermentative processes caused by bacteria already present in the intestinal tract. Often this is caused by the use of milk mixtures that are too strong and therefore indigestible. Every attempt at correcting such diarrhœa by modifications of the milk may be futile.

Diarrhœas due to milk may be the result of the action of bacteria present in the milk, or may more directly result from poisoning by bacterial products present in the milk. The latter forms are particularly severe and more properly merit the term milk poisoning, which is often used in a general sense to indicate diarrhœal disease due to milk feeding. Investigations have shown the presence of an organism closely allied with the *Bacillus dysenteriae* of Shiga in cases of infantile summer diarrhœa of the enterocolitis type. There is little doubt that this organism plays an important part in the etiology of some cases and of occasional extensive outbreaks in institutions or in certain communities. It is quite as certain, however, that cases or outbreaks clinically indistinguishable from these are caused by other microorganisms. Among these are various closely allied organisms differing mainly in their capacity to



ferment different forms of sugar. Other organisms, however, such as the *Bacillus lactis aërogenes*, the *Bacillus coli* and close allies of this group, streptococci and staphylococci are concerned in some cases. In many cases several forms seem to be associated. The most intense diarrhœas of the cholera infantum type seem to be caused by products of bacterial decomposition either occurring in the food or formed in the intestinal tract. No special microörganisms have been connected with these cases.

In older children various other foods may be the cause of attacks of diarrhœa. Unripe or spoiled fruit, particularly, takes high rank. In certain epidemics it has seemed probable that the source of infection was water. The careless use of impure water in the washing of milk cans or bottles may cause infection of the milk, or the drinking water given the child may cause direct infection.

*Age.*—The time of greatest susceptibility is from the sixth to the twentieth month, the period of the primary dentition. Dentition itself, by causing reflex disturbances, excessive secretions, or fever, increases the liability to all forms of diarrhœa, although not the direct cause.

*Season.*—Diarrhœa is distinctly a disease of warm weather, although it may occur at any period of the year. In the summer months it is always more difficult to preserve milk and other foods. In addition, the children are rendered susceptible by free action of the skin and chilling at night.

*Environment.*—Surroundings play an important part. Children in crowded cities and amid surroundings of destitution and squalor are much more liable to severe diarrhœas than those in the country or living under more wholesome conditions. In institutions in which a number of children are in close contact direct infections frequently occur. The greatest care is necessary, in the handling of children, to avoid the communication of diarrhœal conditions; particularly should the handling of the diapers be scrutinized with care. Food standing in the same room may easily become infected, and the preparation of the food should be carried out away from any danger of contamination.

*Pathology.*—The lesions in the various forms of infantile diarrhœa vary considerably; quite commonly the character of the anatomical manifestations is not in keeping with the seriousness of the symptom. Three types may be distinguished, although no sharp dividing line can be drawn between them. These are: (1) simple or dyspeptic diarrhœa; (2) enterocolitis; and (3) choleraic diarrhœa or cholera infantum.

In the first of these the bowel may present no evidences of disease postmortem. When the manifestations have been severe, some indication of catarrhal irritation or inflammation may be found in the upper small intestine and stomach. Congestion, slight thickening, and excessive mucus formation may be discovered. In the enterocolitis of childhood more definite changes in the mucous membrane are seen. Redness and swelling, and frequently enlargement of the lymphatic follicles, are usually met with. Sometimes small follicular ulcerations, and less commonly swelling and slight ulceration of Peyer's patches, may be seen, especially in subacute or chronic cases. In cases of excessive

severity pseudomembranes or extensive ulceration may occur, more particularly in the large bowel. After long-continued attacks of enterocolitis, a thinned, atrophic mucous membrane may be found. Various secondary changes in other organs expressive of depletion of the system occur. In cholera infantum evidences of intense inflammations of the mucous membrane, with exfoliation of epithelium and swelling of the glands and lymphatic follicles, may be seen.

**Symptoms.—Simple or Dyspeptic Diarrhœa.**—Usually evidences of gastric disturbance precede the attack of diarrhœa, and attend it more or less continuously. The child regurgitates food or is attacked by active vomiting. At the same time he becomes restless and distressed, with abdominal pain and distension. The facies and actions suggest griping abdominal pain. Later, diarrhœa sets in, the movements being offensive or sour-smelling, and characteristically containing undigested food, such as curds of milk, together with more or less mucus. The color of the stools varies greatly, sometimes being white or light colored, at other times green. Lesage, in particular, has shown that chromogenic bacteria are active in producing green stools in certain cases. The number of movements may be merely a slight increase over the normal, or may reach ten or more in the twenty-four hours. In some cases the evacuation of the bowels is closely dependent upon the taking of food, one or more movements quickly following each feeding. In such cases there is apt to be a considerable amount of undigested food in the motions.

The general condition is one of moderate prostration, although frequently there is but little weakness until the diarrhœa has lasted for some time. If long continued, emaciation, pallor, and other signs of depletion are met with.

**Enterocolitis.**—The term inflammatory diarrhœa is also applied to this variety. The symptoms are distinctly more intense, and in marked cases reach high grades of severity. Nearly always the child loses strength rapidly, and when repeated, and especially watery, stools are discharged, extreme prostration may speedily occur. Fever is practically always noted, and in severe cases is very high. Temperatures ranging from 103° to 105° are not unusual, and hyperpyrexia is a common manifestation of the enterocolitis of the hot summer season.

The *onset* is usually abrupt, and is attended with evidences of general distress, and especially abdominal pain. Vomiting frequently occurs, but is less conspicuous than in the dyspeptic form, and sometimes, especially in older children, may be wanting. Often, however, obstinate vomiting is a marked symptom. The *stools* are numerous, and vary in color from brown to green. After the contents of the bowel have been evacuated, more watery movements, with less and less color, may occur, so that the condition approaches, in the character of the discharges, to the choleraic type. When the large bowel is especially involved, considerable mucus may be mixed with the discharges.

The general condition of the child is one of rapid exhaustion. The face becomes pinched, the eyes grow hollow and are surrounded by circles, the temples are sunken, and when severe exhaustion has developed the hands and feet may grow cold and cyanosed, while the internal

temperature as determined in the rectum remains excessively high. The abdomen is often distended and the skin tensely drawn and harsh. The child becomes more and more feeble, its movements less active, its cry more and more faint, and its lips dry. Finally, it sinks into a state of complete collapse. An apathetic, stuporous, or even comatose condition, now and then interrupted by a cry, betokens a condition resembling that of meningitis and designated as spurious hydrocephalus.

In cases involving the large intestine to a considerable degree, violent straining occurs with each evacuation of the bowels, and prolapse of the rectum is not unusual. In all cases the bowel movements may be irritating and cause inflammations of the skin about the anus or buttocks. The urine early becomes scanty, and occasionally the secretion is almost suppressed. Actual nephritis occurs in the intensely infective cases.

When the temperature remains persistently high, various nervous symptoms, such as restlessness, slight twitching, and even convulsions, may occur; but the tendency to prostration usually supplants all other nervous indications, and the child sinks into a condition of lethargy or coma. The loss of flesh and strength sometimes increases with startling rapidity. Complications, such as bronchopneumonia, hyperpyrexia, and extreme nervous symptoms, often precede the fatal termination, but more commonly this results directly from exhaustion.

*Diagnosis.*—The recognition of this form of diarrhœa offers little difficulty. In the beginning, high fever and the absence of characteristic intestinal manifestations may suggest infectious diseases of various sorts, but usually the characteristic symptoms speedily present themselves. It is practically impossible to separate cases due to ordinary causes from instances of epidemic diarrhœa produced by the *Bacillus dysenteriae*, except by bacteriological methods.

*Prognosis.*—Enterocolitis is always a serious disease in childhood, particularly in young infants. Older children more commonly exhibit enough resistance to withstand the attacks.

**Choleraic Diarrhœa or Cholera Infantum.**—This form, usually met with in early infancy, is of the most extreme gravity. The onset is sudden, and the child becomes prostrated very early. After a few movements, in which the bowel contents are evacuated, a choleraic form of diarrhœa occurs, the stools being large and watery, and containing but little fecal matter. The whole body undergoes a rapid shrinking, and the features present the shrunken, hollow appearance described as occurring in the most violent cases of enterocolitis, but coming on with even greater rapidity. Extreme dryness of the tongue and mouth and excessive thirst are evidences of the desiccation. The urine is scanty or suppressed. The blood becomes inspissated, and the circulation is interfered with, so that cyanosis of the hands and feet, or of the whole surface, becomes marked. The eyes sink in their sockets, the fontanelle is depressed, and within a few hours the child's face assumes the wrinkled appearance of senility. The surface is cold, and stupor or coma develops rapidly. The surface temperature is greatly reduced, while the internal temperature, as observed in the rectum, may rise to 105° or more.

The course is brief, and in a large proportion of cases terminates



fatally. When improvement occurs there is a subsidence of temperature, a gradual cessation of diarrhœa, and a slow restoration of strength. Not rarely a less degree of diarrhœa persists for some time, due to a residual enterocolitis.

**PROGNOSIS.**—The mortality from this form is exceedingly great. When it occurs in institutions containing large numbers of infants, a fatal termination may take place in above 90 per cent. In older children the outlook is less grave, although it is always a condition of extreme severity.

**Treatment.**—The prophylactic treatment is of the greatest importance. Greater care in the preparation and preservation of food and increased knowledge of the causes of diarrhœa have led to a decided diminution in the frequency of these conditions, although much remains to be accomplished. In hot seasons of the year all forms of food, but particularly milk, should be kept with the strictest care. When children are bottle-fed, the food if prepared in the morning for the whole day should be kept in a refrigerator. Careful pasteurization is often necessary when the freshness of the milk is doubtful. In the early morning some other form of food, such as barley-water or prepared foods, may be used with advantage until the new supply of the day has been received. In the cases of older children rigid care should be taken to avoid the use of stale foods of all sorts.

The susceptibility of the child may be lessened by the avoidance of exposure. In the summer, when the nights are relatively cool, care in the dress is of importance, particularly the protection of the abdomen and legs. Infectious diarrhœas may be avoided in institutions by the separate management of the children and by the closest care in the handling of the napkins.

**Medicinal.**—After the onset, treatment should be directed to the removal of irritants, the control of the diarrhœa, and the support of the patient's strength. In the milder dyspeptic diarrhœas the prompt administration of a dose of castor oil and the withdrawal of the accustomed food, substituting for this barley-water, rice-water, albumin-water, weak broths and the like, may speedily terminate the condition. If the tendency to diarrhœa persists, mild astringents, such as powders of bismuth subnitrate, subgallate, or subcarbonate, with or without the addition of pepsin, may be sufficient. More active astringents, like chalk mixture with kino or catechu, and tannic acid preparations of other sorts, may be used. Frequently, small doses of calomel, alternating with bismuth, chalk mixture, or other astringents, appear to have a good effect. When the movements are acid and irritating, alkalis, such as magnesia, soda, or lime-water, may be employed.

In cases of enterocolitis, preliminary purgation may be desirable, although it must be used with greater caution than in the dyspeptic diarrhœa, because the tendency to spontaneous evacuation of the irritating matters in the bowel is greater and prostration is more imminent. Sometimes, however, the prompt administration of castor oil or magnesia is desirable. When vomiting is severe, all food should be withheld for a time, or only diluted barley-water, rice-water, or thin

gruel given. At the same time, small doses of calomel, alternating with bismuth powder, may be employed. In later stages, astringents, such as have been mentioned before, are useful. Opium in the form of laudanum, Dover's powder, or paregoric is often necessary to check obstinate diarrhœa; and sometimes, when violent purgation threatens speedy collapse, a hypodermic injection of morphine (gr.  $\frac{1}{50}$  to gr.  $\frac{1}{20}$ , gm. 0.0013 to 0.003) may exercise a rapid controlling effect.

When the temperature is high and prostration is severe, colonic irrigations are most serviceable. With the hips elevated, the colon may be flushed without exciting irritation of the bowel, and the effect upon the general condition of the child is frequently surprising. The water used for irrigations should be of a temperature of from 90° to 80° or 75° F.; the amount may vary, according to the age of the child, from half a pint to a quart. A catheter or small-sized rectal tube, passed high into the bowel, and a fountain syringe, elevated not above a foot or two, suffice for the injections. If the colon and rectum are irritable, the first injection may be at a higher temperature; and a few drops of laudanum may be added to the fluid. Sometimes a small amount of oil or a little starch-water containing laudanum, cocain, or other sedatives, may be injected first. In later stages, if colitis persists and slight diarrhœa with abundant mucus continues, injections of fluid extract of hamamelis in normal saline solution (1 to 65) or nitrate of silver (1 to 8000) may be employed. Stimulants and other supporting measures may be necessary; hypodermics of strychnine (gr.  $\frac{1}{400}$  to gr.  $\frac{1}{200}$ ) and small doses of brandy, tincture of digitalis, or tincture of nux vomica may be used. If the external temperature has remained high, sponging or cold packs may be employed with advantage.

In *cholera infantum* the tendency to speedy collapse requires the prompt administration of stimulants. External heat may be needed when the surface temperature sinks, and injections of fluid under the skin may be necessary to counteract the loss of water. The diarrhœa may be controlled by the use of astringents administered as freely as the condition of the stomach permits. In many cases the prompt administration of a hypodermic injection of morphine will check vomiting and diarrhœa, and permit of the administration of other remedies. When the diarrhœa is under control the cautious increase of nourishment and the use of stimulants are required to restore the patient's strength. The greatest care must be taken to prevent a recurrence of the intestinal disturbance.

Serum treatment has been employed since the discovery of organisms resembling the bacillus of Shiga in cases of infantile diarrhœa, but the results have not proved encouraging.

### ULCERATION OF THE BOWEL

A classification of intestinal ulceration is difficult, and from many standpoints unsatisfactory. The most rational is that of Nothnagel:

*First Group.*—Ulceration as the result of necrotic processes: Simple duodenal ulcer (including peptic ulcer of the jejunum); ulcer following

cutaneous burns; embolic and thrombotic ulcer (the peculiar ulcers seen in patients with multiple neuritis belong to this class); amyloid ulcers.

*Second Group.*—Ulceration as the result of inflammatory processes: Catarrhal ulcer; follicular ulcer; simple ulcerative colitis; stercoral or decubital ulcer.

*Third Group.*—Ulceration as the result of acute infectious diseases: Typhoid; dysentery; diphtheria; anthrax; sepsis; erysipelas; varioloid.

*Fourth Group.*—Ulceration as the result of chronic infectious diseases: Tuberculosis; syphilis; erysipelas; leprosy; pellagra.

*Fifth Group.*—Ulceration as the result of constitutional diseases: Gout; scurvy; leukemia.

*Sixth Group.*—Toxic forms of ulceration: Uremic ulcer; mercurial ulcer.

**Duodenal Ulcer.**—The duodenal mucous membrane is frequently the seat of ulceration resembling that found in the stomach, and known as gastric or peptic ulcer. The form under consideration is that which results from digestive action rather than from infectious, toxic, or inflammatory processes. It has been designated simple duodenal ulcer or peptic duodenal ulcer.

**Etiology.**—Duodenal ulcer is found associated with certain diseases, notably of the stomach. As to the association of gastric with duodenal ulceration, according to the Fenwicks, 1.7 per cent. of cases of gastric ulcer were accompanied by a lesion of the duodenum, but Mayo and Moynihan have found that half their cases of duodenal ulcer were associated with gastric ulceration. The clinical history of cases indicates that chronic gastritis with excess of acid secretion is a factor of considerable importance in the development of duodenal ulcer. Nearly all patients give a history of antecedent gastric disorders.

In recent years some surgeons have maintained that chronic appendicitis is a common cause of gastric and duodenal ulceration. The exact mode of operation, however, is uncertain.

Ulcer of the duodenum is more common in men than women and occurs most frequently in the third and fourth decades.

Duodenal ulceration appears to be associated with tuberculosis rather more frequently than it is found in persons free of this disease or suffering with other maladies. Ulceration of the duodenum has also been referred to as occurring in chronic nephritis. These ulcers, however, are somewhat different in their general character from ordinary duodenal ulcers. Extensive burns of the skin are associated with duodenal ulcers, but these differ in character and causation from true duodenal ulcers.

**Pathology.**—Duodenal ulcers, like those of the stomach, may be distinguished as acute or chronic. The former are circular and punched-out in appearance, and the floor and edges are congested and soft. The chronic or indolent ulcer presents thickened, indurated, and sometimes undermined and irregular edges, and not infrequently has a sloping form, which gives the ulcer a funnel shape. Acute ulcers may be quite superficial, presenting themselves as mere erosions of the mucous membrane. The more chronic forms are deeper, extending to the submucous or even to the muscular coat, and occasionally penetrating through all



the coats, when the liver, the head of the pancreas, or some other neighboring structure may form the floor of the ulceration, adhesions having prevented an open rupture into the abdominal cavity. The mucosa surrounding an ulcer, although usually normal, may present evidences of irritative change, and is sometimes irregularly elevated or polypoid. Microscopically the floor and edges of the ulcer present necrotic changes, with some increase in connective tissue, but without the evidences of active inflammatory conditions, such as are found in ordinary ulcerations.

The situation of duodenal ulcers is usually in the first part of the duodenum, near to the pylorus. The majority of the ulcers in the first part of the duodenum are situated quite near the pylorus, and are deepest at the upper part where the gastric contents are projected with greatest force against the duodenal wall. The anterior wall of the duodenum seems to be affected more frequently than the posterior, although observers do not agree upon this point.

*Secondary Changes.*—Duodenal ulcers may undergo a process of gradual cicatrization; but apparently this termination is less common than in gastric ulcers. Chvostek insists that cicatrization is more common than has been generally believed. Perry and Shaw estimate it as occurring in 11 per cent. of all cases. When it occurs there may result a stenosis or deformation of the duodenum similar to the stenoses produced by cicatrizing gastric ulcers. Progressive dilatation of the stomach with symptoms of food stagnation result. Cicatricial stenosis of the lower end of the duodenum or the parts adjacent to the papilla of Vater may occasion obstruction of the biliary and pancreatic ducts. Occasionally diverticula of the duodenum follow the cicatrization of an ulcer. Deep ulcers may cause severe hemorrhage, from involvement of the large arteries adjacent to the duodenal wall.

*Perforation* of the duodenum occurs in about half the fatal cases. Ulcers upon the anterior wall are more apt to terminate in this way than are those upon the posterior wall, owing to the absence of adhesions. When a perforation takes place without the previous formation of any adhesions the contents of the stomach and duodenum have ready access to the peritoneal cavity, and usually occupy the right side of this sac, extending along the colon toward the pelvis. When adhesions have formed, or when the perforation is minute, a localized abscess may develop. In such cases secondary perforation of the abscess into the liver, the stomach, other portions of the intestines, or the gall-bladder, or through the diaphragm into the pleura, the mediastinum, or the pericardial sac, may occur. In a few instances, rupture into the aorta, portal vein, vena cava, or gall-bladder has been recorded.

*Symptoms.*—In a large proportion of cases duodenal ulcers are chronic in course and the symptoms are slow in development. Occasionally acute ulceration occurs, and the symptoms make their appearance suddenly, intense pain and acute disturbance of digestion, followed by the rapid development of hemorrhage or perforation, being met with. In the great majority of cases, however, such acute onset is wanting, the symptoms being slow in development and without characteristic significance in the earlier stages. In these cases the patient suffers with

gastric manifestations and resulting emaciation, loss of strength and appetite, and finally attacks of pain suggesting hyperacidity. Very commonly the clinical course of duodenal ulcer is characterized by periods of active symptoms followed by remissions, in which complete relief from all discomfort and restoration of strength and normal weight occur. In many instances the condition may be entirely latent until hemorrhage or perforation take place, and cicatrices of old duodenal ulcers may be found at autopsy in cases in which no evidences had been manifested during life to indicate the disease. The most marked symptoms are pain, dyspeptic manifestations, and hemorrhage.

The *pain* is frequently paroxysmal, like that of gastric ulcer. It may be of intense severity or merely a dull discomfort at certain periods after the ingestion of food. In other cases, whether severe or dull, it is more lasting, and sometimes a constant sense of burning or of sharp pain is experienced. The pain is situated to the right of the middle line, and usually a little above the umbilical level. It may radiate toward the right, or in other cases extend toward the left side. Sometimes it is described as having a deep-seated location, being rather unlike the characteristic pain of gastric ulcer in this particular. The time of its appearance varies. Sometimes it follows immediately after the taking of food, but more commonly it does not occur, or does not reach its acme, until two, three or four hours after meals. The character of the food may have a certain relation to the occurrence and the intensity of the pain. Generally speaking, heavy meals occasion more severe pain; although it may be somewhat later in appearing. The drinking of copious draughts of water or the taking of other liquids, such as milk, beer, wine, etc., may relieve the paroxysm for a time.

Tenderness and rigidity of the abdominal muscles may be met with over the seat of duodenal ulcers, especially those situated anteriorly. Pressure usually increases the pain, although not invariably.

*Gastric* symptoms are rarely wanting in typical cases. In a great many instances there is a history of long-standing gastric disturbance. The patient will state that he has gone from one form of diet to another in the vain endeavor to relieve himself of recurring pain after the ingestion of food. The symptoms usually complained of are gaseous distension, acidity, the regurgitation of sour liquid, and especially dull or sharp pain after the taking of food. Loss of appetite may occur, but more commonly the patient refuses food or restricts his dietary from the fear of causing pain and other discomfort. In other cases there is an intense craving for food, which is controlled only by the pain that follows its ingestion. Vomiting sometimes occurs. The general condition of the patient is suggestive in the later stages. He is emaciated, sallow, or anemic in appearance, the latter being striking when a slow and continued oozing of blood has occurred; and frequently he presents a desiccated, shrivelled appearance. The bowels are usually constipated, but may be variable, short attacks of diarrhœa alternating with longer periods of constipation. Often constipation is the most marked symptom presented. Examination of the stomach contents shows hyperacidity and excess of free hydrochloric acid in perhaps a half of all cases, with normal or moderate acidity

in most of the other half. Exceptionally a quite low acidity may be found. The symptoms suggestive of hyperacidity are not always found associated with actual excess of acid.

*Hemorrhage* may occur from the stomach or from the bowel, or the blood may be evacuated in both ways. More frequently than severe hemorrhage there is slight oozing of blood, which may occasion a discoloration of the stools that is just sufficient to be observable; or there may be so little blood that it can be recognized only by chemical tests (occult blood). The continuous presence of small amounts of blood, when associated with suggestive symptoms, is a diagnostic indication of great value.

*Perforation* of a duodenal ulcer may occasion symptoms similar to those met with in the perforation of gastric ulcers. Usually the onset of this complication is attended with sudden prostration and pain. The patient may sink at once into a condition of shock or collapse; later he may revive and pain in the abdomen, especially toward the right side, tenderness, and distension, due to the development of peritonitis, may then set in. In a great many instances the diagnosis of appendicitis has been made, on account of the acuteness of onset and the tendency to right-sided situation of the symptoms.

**Complications.**—Among the complications are those which result from extension of the ulcerative process through the duodenal wall, and those which are due to cicatrization of the ulcerated area. In the former group, the most important condition is localized peritonitis. In the case of slowly growing ulcers a certain amount of localized peritonitis, causing adhesion with neighboring organs is frequent. When these adhesions fasten the duodenum firmly to some solid structure and the ulceration penetrates to the serous coat, a localized abscess may occur; or a further penetration into the various structures with which the duodenum has become adherent may take place.

Among the results of cicatrization of the ulcer the most important is partial stenosis of the duodenum, which, in turn, occasions an enlargement of the stomach. Occasionally, when the ulceration has been situated near the papilla of Vater, obstruction of the common bile duct may occasion jaundice or an obstruction of the pancreatic ducts.

Carcinomatous change may take place secondarily and clinical indications of carcinoma may be recognized.

**Diagnosis.**—A positive diagnosis of duodenal ulcer is frequently impossible. In particular, the distinction from gastric ulcer cannot be made with certainty. This is of minor consequence, as an ulceration just within or just outside the pyloric ring is, to all intents and purposes, of the same consequence. Duodenal ulcer must also be distinguished from gall-stones and occasionally from chronic appendicitis. Reflex hyperacidity and gastritis may simulate ulcer very closely.

The history of long-continued digestive disturbance with occasional remissions is of some importance in the diagnosis. The most suggestive symptoms upon which a diagnosis is usually established are pain and gas, occurring from two to four hours after meals and often at quite a fixed hour in the night, and not rarely yielding temporarily when food



or an alkali such as bicarbonate of soda is taken; sour stomach; belching, nausea and later vomiting; constipation.

Fluoroscopic and skiagraphic examinations show active peristalsis with discharge of the bismuth in large masses; persistence of the duodenal cap; later distinct gastric retention. Not rarely, however, the stomach throughout the case shows premature emptying of its contents. In cases of gastric ulcer the symptoms are less remitting, the pain occurs earlier after the taking of food and is often higher up and more superficial; nausea and vomiting are more pronounced, at least in the earlier stages.

Gall-stones frequently occasion gastric symptoms very similar to those of ulcer, but the intensity of pain is greater, its relation to food usually less definite, and the relief from taking food less frequent. Jaundice and tenderness in the right hypochondriac region are more common.

Sudden rupture of a duodenal ulcer, with resulting peritonitis, may be mistaken for appendicitis, intestinal obstruction, acute pancreatitis, and sometimes cholelithiasis. The tendency of the pain and tenderness to extend to the right, and thus suggest appendicitis, should be noted.

The withered, emaciated condition of a patient who has had long-standing ulceration of the duodenum may suggest the existence of carcinoma at the pylorus, particularly when pyloric spasm, constant or paroxysmal, has occasioned enlargement of the stomach and visible peristalsis. There may even be a palpable mass due to periduodenal adhesions and inflammation. In such cases a positive diagnosis is sometimes impossible.

**Treatment.**—This is practically identical with that of gastric ulcer. In acute cases, prolonged abstinence from feeding by the mouth is the most important element. The patients can, without difficulty, abstain from all food for days or a week or more; some nourishment, perhaps, being derived from nutrient enemata and water being administered by the bowel; later, carefully regulated diet composed of milk, eggs, farinaceous foods. Subsequently, moderate additions of meat and vegetables as free as possible from irritating residues may be added. Such a dietary should extend over a period of several weeks and should be increased very gradually. Bismuth subnitrate, olive oil, or nitrate of silver may be given by the mouth for the purpose of neutralizing acidity, protecting the ulcerated surface, and through an astringent effect stimulating cicatrization. If bismuth is used and complete starvation is practised, small doses will suffice, gr. 10 to 15 (gm. 1) being administered several times daily in suspension. Olive oil, in doses of from 2 drams to  $\frac{1}{2}$  ounce or 1 ounce, may be given several times daily; and nitrate of silver, in solution in distilled water, or in the form of freshly made pills. The doses of this drug should be small, not exceeding gr.  $\frac{1}{4}$  (gm. 0.016), and preferably administered a number of times daily, rather than large doses at longer intervals. Belladonna or atropine in full doses is decidedly efficacious in controlling hyperacidity and pyloric spasm.

Occasional lavage of the stomach with plain water, or with water containing bicarbonate of soda may have a temporarily useful effect; but, as a rule, lavage should be avoided.

In less acute cases a more prolonged treatment of the same sort, with

very carefully moderated feeding by the mouth, may prove successful. As a rule, however, subacute and chronic ulcers of the duodenum tend to persist, and eventually will require surgical treatment. It is wiser, therefore, to resort to surgical measures as early in such cases as a positive diagnosis is made. When perforation of a duodenal ulcer takes place, immediate surgical operation is imperative.

**Duodenal Ulceration following Extensive Cutaneous Burns.**—As yet no satisfactory explanation for the relationship of the two phenomena has been presented. Theories that would rationally explain the occurrence of intestinal ulceration after extensive burns have been advanced, but none satisfactorily explains the fact that the duodenum alone is usually the seat of the phenomenon. From this standpoint the theory proposed by Hunter is the most rational. He explains the condition by assuming that, following the burns, toxic substances are secreted with the bile, which, on coming in contact with the duodenal mucous membrane, induce ulceration. He found substantiation for this view in the experimental occurrence of duodenal ulceration after the subcutaneous injection of toluylendiamin into dogs. However, Fenwick was able to produce the same lesions on repeating the experiment after ligation of the common bile duct. Another view is that the condition is a result of emboli localizing themselves in the duodenal vessels, thus lowering the nutrition of the parts involved and subjecting them to digestion by the gastric juices. Cooke offers the theory that the violent trauma to the skin destroys the antiferments present in the mucous cells, and as the digestive powers of the gastric juice are most potent in the duodenum, digestion of the mucous membrane occurs here. A discussion of the various theories has been presented by Bardeen.<sup>1</sup>

The ulcers differ in many features from the peptic duodenal ulcers. There may be but one ulcer or from three to six present. They are usually located in the inferior horizontal portion of the duodenum. They may be irregular in outline or, as is usually the case, are long and narrow, varying in width from 1 to 5 mm. and in length from 5 to 15 mm. In exceptional cases, ulcers in the stomach or the lower part of the intestinal tract have been found associated with such duodenal ulcers. Usually the ulcer develops from the sixth to the twelfth day after the burn, but they have occurred as early as the second day and as late as the seventeenth. They are met with chiefly in young subjects, rather oftener in females than in males and more frequently after burns of the trunk than on the extremities. They are almost invariably fatal. According to the Fenwicks they occur in 6.2 per cent. of all fatal burns.

**Jejunal Peptic Ulcer.**—Jejunal peptic ulcer occurs after gastrojejunostomy from the same causes that induce duodenal peptic ulcer. It occurs just beyond the point of attachment of the jejunum to the stomach. For some unexplained reason this condition is met with much more frequently in males than in females. Of 31 cases collected by Gorset, 29 were males. Jejunal ulcer results more commonly from anterior than from posterior gastrojejunostomy. This probably results from the fact

<sup>1</sup> *Journal of Experimental Medicine*, vol. ii, p. 501.

that the motor activity of the stomach is less impaired in the posterior operation, and consequently there is a lessened tendency to hyperacidity, which is the important factor in the production of the ulcers. Jejunal ulcer manifests the same tendency to perforation as does duodenal ulcer, but the resulting peritonitis is more frequently circumscribed. According to Mayo Robson, general peritonitis is more likely to follow perforation after posterior gastrojejunostomy than after the anterior operation.

**Uremic Ulcers.**—Difference of opinion prevails as to the probable cause of this ulceration. It has been variously attributed to capillary thromboses, to arteriosclerosis of the intestinal arteries, and to submucous hemorrhages. In all probability the excretion of irritating substances into the intestinal tract is more or less responsible. A feature lending considerable weight to this view is the fact that in the vast majority of cases of nephritis some degree of catarrhal enteritis is found, undoubtedly caused by the irritation of excretory products; and various degrees of catarrhal and even diphtheritic enteritis are usually associated with the ulceration. The ulcers are most frequently found and most numerous in the rectum, colon, and lower ileum, although occasionally they are almost or entirely limited to the duodenum. They vary greatly in size. The smaller ones have regular and somewhat undermined edges. They frequently coalesce, forming large, irregularly outlined areas of ulceration. The condition is usually met with in chronic interstitial rather than in the parenchymatous forms of nephritis.

**Embolie and Thrombotic Ulcers.**—The intestines are subject to changes dependent upon alterations of the blood supply, just as other tissues. The resulting lesions are dependent not only upon the character of the obstruction but also upon its extent. If a large arterial branch be occluded so as to alter seriously the blood supply of a considerable part of the intestine, phenomena will result, which are discussed elsewhere. If smaller branches be occluded, especially those running in the intestinal wall itself, ulceration will often ensue. Although thrombosis induced by sclerotic changes in the vessel walls may be the cause of such lesions, a much commoner cause is embolism. The character of the lesion in the intestinal wall will depend upon the character of the embolus, whether it be bland or infectious.

If an embolus occludes one of the smaller branches of an intestinal vessel, a hemorrhagic infiltration of the submucous tissues soon develops and later extends to the mucosa. The area involved becomes swollen, firm, and dark or grayish red. The tissues in the area of distribution of the vessel soon become necrotic, and the mucous membrane with more or less of the underlying tissues is cast off and an ulcer results. Usually the central portion of the area involved shows the most advanced changes. Frequently the visceral peritoneum corresponding to the area of involvement is the seat of a hemorrhagic infiltration. If the occlusion has been such that the entire thickness of the wall is involved, the ulcer becomes much deeper and early perforation may result. Usually the ulcers are of small size and involve only the mucous membrane and submucosa. They are usually multiple. If the embolus be septic, a localized submucous infiltration of leukocytes occurs and a small abscess forms.



This increases in size and finally ruptures into the intestinal lumen. If the involvement of the wall be more extensive, perforation may occur and peritonitis result.

**Catarrhal Ulcers.**—However inappropriate this term may be, it expresses well enough the nature of the condition—an ulceration occurring in conjunction with and apparently the result of catarrhal inflammation. It is seen especially in catarrhal enteritis of rather long duration, and more frequently in children than in adults. The ulcers are present in both the small and large intestines, but are more numerous in the latter. They are usually minute, round ulcers with very slightly indurated edges. Larger ones may occur which are frequently the result of the confluence of several small ulcers. These larger areas generally have an irregular outline. The ulceration usually involves only the mucous membrane, and at times not even its entire depth. The ulcers are usually numerous, and at times the process is so extensive that only islands of mucous membrane are left between the ulcerated areas. The mucous membrane that remains free of ulceration is the seat of catarrhal inflammation. Since the process is limited to the mucous layer, perforation practically never occurs; but it is not unusual to find various degrees of cicatrization when the condition shows a tendency to heal.

The mode of formation of catarrhal ulcers has been the subject of some discussion. The specially mooted question has been whether the primary stage of the process is in the mucosa itself, inducing ulceration by direct action upon the epithelium, or whether there is originally a submucous infiltration inducing ulceration by interference with the nutrition of the overlying parts. Since the catarrhal changes preceding the ulceration are most marked in the mucous layer, and since only the most superficial portions of the mucosa may be ulcerated, the former theory is the more rational.

**Follicular Ulceration.**—This occurs as a result of the same conditions that induce catarrhal ulceration. In the latter condition the mucous membrane is the portion specially affected, whereas in follicular ulceration the solitary lymphatic follicles are the seat of the process. The inflammation induces a hyperplasia of the lymphatic elements of the follicles which later undergo central softening. The swelling of the lymphatic follicles interferes with the nutrition of the overlying mucosa and subjects it to mechanical irritation, so that it undergoes necrosis, and the softened elements of the lymphatic follicles escape, leaving an ulcer. As the extent of the follicle is usually greater than the area of superficial ulceration, the resulting ulcer has usually a more or less undermined edge. The ulcers are usually numerous, at times giving a typical honey-comb appearance to the part involved. Perforation seldom occurs. The colon and lower ileum are much more frequently the seat of the process than the upper portion of the intestinal tract, and the condition is more common in children than in adults.

**Stercoral or Decubital Ulcers.**—These result from the irritant action of inspissated fecal masses on the intestinal wall. This action may be purely mechanical, or, what is more probable, the mechanical injury to the mucosa serves only as the occasion for ingress of pathogenic

organisms. The condition naturally is found only in the large intestines, and especially at the points where stagnation occurs, at the hepatic and splenic flexures, in the rectum, sigmoid, cecum, and appendix. The ulcers are usually circular in outline and have an inflamed suppurating base. The condition is more frequently met in elderly individuals subject to constipation. Perforation of a stercoral ulcer has been known to occur. Not infrequently these ulcers lead to cicatrization and stenosis, and Grawitz remarks that probably not infrequently these stenoses have been mistaken for carcinomatous strictures, while Nothnagel calls attention to the possibility of carcinoma developing as a secondary manifestation in the edges of the cicatrices.

**Leukemic Ulcers.**—In leukemia, and especially in the more acute form, it is possible for lymphatic hyperplasia in the intestinal wall to occur of such a degree as to induce ulceration of the overlying mucous membrane. Such ulcers are more commonly found in the ileum than in other portions of the intestinal tract, although usually some other portions of the digestive tract, especially the mouth and pharynx, are involved.

**Trophic Ulcers.**—In various nervous and mental disturbances, ulceration of the intestines has been observed. Nothnagel refers to cases reported by Kussmaul and Maier, Minkowski and Lorenz, in which extensive intestinal ulcerations occurred in conjunction with multiple neuritis. In most of these cases sclerotic or thrombotic changes in the vessels were found, so that Nothnagel concludes that the intestinal lesions were the result of the vascular changes associated with the neuritis. Others consider it possible for the intestinal ulceration to result from disease of the brain and spinal cord. The cases of Targett and Ogle are particularly striking. In both of them there was fracture of the spine followed shortly after by diarrhœa, and at autopsy extensive ulceration of the colon was found. It is not improbable that these lesions were the result of the same factors inducing the superficial trophic ulcerations so common in spinal disease.

**Symptoms of Intestinal Ulceration.**<sup>1</sup>—There may be a complete absence of symptoms, even in cases of extensive ulceration, especially when the lesions mainly occupy the small intestine. When the colon is involved, and particularly when its lower portions or the sigmoid and rectum are affected, symptoms are less frequently wanting. Even in these cases, however, there may be a striking absence of clinical manifestations. Among the symptoms in the different forms of ulceration of the bowels, diarrhœa, hemorrhage, or the passage of small amounts of blood, the discharge of pus and shreds of tissue, anemia, pain, fever, and general disturbances of health are the most important.

*Diarrhœa* is perhaps the most frequent symptom and is caused by the direct irritation of the intestinal nervous mechanism by the ulcerative process or by interference with intestinal absorption. Its character varies with the location of the ulcers. When these are situated in the small bowel, in the cecum, or in the upper portions of the colon,

<sup>1</sup> Duodenal ulcer, tuberculosis, and syphilis, as well as the ulceration of specific infections are excluded.

diarrhœa, if present, is of the ordinary kind with more or less fluid or unformed movements. No special characters distinguish the diarrhœa in such cases from that in simple irritation or catarrhal conditions. When the lower part of the large bowel is the seat of the ulcers, there is a greater tendency to admixture of mucus and blood, and the diarrhœa partakes of the nature of dysentery in proportion to the intensity and extent of the ulcerative processes. Intense straining at stool or tenesmus is sometimes met with in such cases, and marked soreness or tenderness over the descending colon or sigmoid flexure may occur.

*Hemorrhage* is less common in the forms now under consideration than in simple duodenal ulcer and typhoid ulceration. Sometimes, however, considerable hemorrhage or the passage of blood with each stool may occur, especially when the ulcers are in the lower bowel. Small amounts of blood and occult bleeding are more common. When sloughing attends extensive ulceration, blood, pus, and shreds of tissue may be passed together. Pus and portions of tissue are highly suggestive of ulcerative processes. They are more common in cases of dysentery than in other ulcers, but may occur in any extensive form of ulceration. When intestinal ulceration is attended with large or repeated hemorrhages the patient becomes highly anemic. In the earlier stages, and especially after large hemorrhages, the anemia has the ordinary characters of posthemorrhagic secondary anemia, but in cases of long-continued slight bleeding a more intense anemia results, and often one of a type that is highly suggestive of pernicious anemia.

*Pain* is a symptom of no regularity of occurrence. Closely grouped ulcers in the sigmoid or rectum are commonly attended with marked local tenderness and pain of a constant or paroxysmal colicky type. Ulcers elsewhere in the bowel are less frequently attended with pain, and those in the small intestine rarely cause greater discomfort than that of occasional attacks of colic or vague soreness in the abdomen. When the ulcers are in the rectum or sigmoid, tenesmus may be pronounced.

*Fever* is less pronounced than might be expected. In stercoral and catarrhal ulcerations some degree of fever is usual, and at times it becomes marked. In other forms it is not regularly present.

The general condition of the patient is by no means indicative of the presence or degree of ulceration. Sometimes, despite extensive lesions, the patient presents no evidence of great disorder of health. In other cases, especially when diarrhœa, fever, and hemorrhage occur, there may be emaciation, loss of strength, and severe anemia.

**Diagnosis.**—It is extremely difficult to recognize intestinal ulceration in many cases. The occurrence of diarrhœa, the discharge of blood or pus and blood, and local pain or tenderness are highly suggestive symptoms. When ulcers are situated in the rectum or sigmoid region they are readily demonstrable with the enteroscope. It may be doubted, however, whether the routine use of this instrument is advisable. Injuries to the ulcerated areas, even perforation of the bowel, have occurred in expert hands, and the cases in which a diagnosis can be made with certainty by the aid of the enteroscope are usually cases in which it can be made with almost equal certainty without this instrument.



**Prognosis.**—Ordinary intestinal ulcers tend to heal in time, provided the proper hygienic, dietary, and medicinal measures are adopted. In cases in which extensive ulcers of the large bowel are present there is, however, a likelihood of great obstinacy to treatment. When extreme anemia and emaciation have occurred the prognosis is rather unfavorable.

**Treatment.**—The treatment of ulcers in the upper part of the intestinal tract does not differ from that of diarrhoea due to other conditions. Careful regulation of diet, rest, local warmth and protection of the abdomen, mild astringents, such as bismuth salts, chalk mixture, vegetable preparations containing tannic acid, nitrate of silver, or salts of lead, are the remedial measures.

Ulcers in the lower bowel can often be treated with advantage by injections or by direct topical applications through an enteroscope. Among the useful forms of injection may be mentioned solutions of nitrate of silver (1 to 5000 to 1 to 1000), weak solutions of salicylic acid, boric acid, thymol, or other antiseptics, astringent lotions, or flushings with simple salt solution. Sometimes nightly injections of an ounce or several ounces of olive oil may be advantageous. In conjunction with such measures the regular use of mild laxatives is useful in preventing the formation of scybalous masses.

Direct treatment of the ulcers with stronger solutions of nitrate of silver and other astringents, suspensions of iodoform, and various antiseptics, may prove effective in cases of limited ulceration which can be reached through the enteroscope.

### PERICOLITIS

Occasionally inflammation occurs in the tissues surrounding the colon resembling periceal and peri-appendicular inflammation.

**Etiology.**—The causes are numerous. Sometimes it results from direct injury; at other times, from organic lesions within the colon or perforation by foreign bodies. Probably in the majority of cases obstinate constipation and stercoral ulceration are the causes of extension and involvement of the tissues surrounding the colon. Various foreign bodies, such as pieces of bone, needles or pins, fragments of straw or wood, and the like, have been discovered penetrating the wall of the colon or lying in an abscess that has formed outside. Attention is called, in the section on Diverticula, to the occurrence of inflammations within and surrounding such extensions from the bowel.

**Pathology.**—Whatever the original cause of the condition, the resulting lesions are similar, although varying in extent. Sometimes there is merely an inflammation or ulceration within and some reactive inflammatory thickening on the outer surface of the bowel. When more extensive destruction of the mucosa has occurred, or when complete penetration by a foreign body or perforation has taken place, more extensive external inflammation occurs. This may result in a chronic inflammatory thickening; or, if active infection has occurred, an abscess may follow. Sometimes, as Bland-Sutton has shown, such abscesses

may discharge into the bowel, and the tumor, which was before palpable, spontaneously disappears. In many cases the final result of the condition is the formation of fibrous thickenings or of adhesions which may attach the bowel to neighboring structures or cause contraction.

The usual situations in which pericolitis occurs are the hepatic and splenic flexures of the colon or the sigmoid flexure. The term *pericolitis sinistra* has been specially applied to cases occurring in the last-named situation. Perityphlitis of cecal origin is practically identical with the condition now under discussion; but, on account of its close relationship with appendicitis, it has been referred to in the discussion of that condition.

Recently considerable attention has been paid to a form of pericolitis in which the colon is surrounded by a veil-like membrane (Jackson's membrane). Some of these cases are probably the result of preceding inflammatory conditions in the bowel and local infection; others are probably developmental in origin.

**Symptoms.**—The clinical manifestations indicate an acute inflammatory trouble with local pain and tenderness on pressure, more or less fever, and disturbance of the function of the bowel. In some cases constipation occurs as the result of inflammatory weakening of the affected segment of bowel or of pressure upon the bowel. In other cases diarrhœa occurs, and sometimes mucus and blood appear in the feces. Sometimes a localized induration or mass may be discovered. In rare instances spontaneous disappearance of the mass may occur in consequence of rupture into the bowel.

**Diagnosis.**—The condition presents practically the same symptoms as those met with in appendicitis. The location of the lesion usually excludes this condition; but the possibility of a misplaced, and even a left-sided, appendix should be remembered. Some cases in which a tumor has been felt through the abdominal wall have been regarded as cases of carcinoma; and the diagnosis has been disproved only after operation or spontaneous recovery. The acute symptoms and the indications of inflammation and infection should aid in excluding carcinoma, when the possibility of pericolitis is borne in mind.

**Treatment.**—The treatment of the condition is purely surgical.

## APPENDICITIS

**Definition.**—In a strict sense the term appendicitis should be used to define inflammations of the vermiform appendix. It has, however, obtained a broader clinical significance, embracing various inflammatory affections of the right iliac fossa with which inflammation of the appendix is associated as a more or less important factor. Formerly the term typhlitis was much in use, and was based upon the idea that inflammations of the region designated originated in the cecum and head of the colon and spread from these structures to the surrounding tissues (perityphlitis). Modern investigations have shown that in the great majority of instances perityphlitis has its origin in primary appendicitis,

and for practical purposes it may be accepted as established that inflammations around the head of the colon originate in the appendix, and should be dealt with as cases of appendicitis. The term appendicitis is sometimes loosely applied to diseased conditions of the appendix, such as cysts, mucocoeles, etc., which are not necessarily inflammatory, although secondary inflammatory conditions may subsequently associate themselves. When used in this way, the term must be recognized as having a clinical rather than a pathological applicability.

Notwithstanding the fact that various surgical writers have denied the existence of primary localized inflammations of the cecum without appendicitis, there is abundant evidence that such a condition does occur. MacWilliams<sup>1</sup> reviewed a number of cases and showed conclusively the existence of both acute and chronic typhlitis independent of appendicitis, tuberculosis, dysentery, cancer, or other like conditions. These forms of typhlitis are due to obscure causes or to coprostitis. The disease of the cecum may go on to ulceration, perforation, and the formation of perityphlitic abscess or general peritonitis, the appendix meanwhile remaining normal. H. A. Kelly has reported 14 such cases. For practical purposes, however, the comparative rarity of this condition justifies the physician in disregarding it, unless the development of the case has strongly suggested the retention of fecal matter in the cecum and the physical signs indicate stasis in that region.

**Anatomy.**—Embryologically the appendix is a derivative of the cecal pouch, originating as a small process from that structure in the seventh or eighth week of fetal life. In the early stages of the development of the intestinal tube the cecum is situated rather high up, near the under surface of the liver, but subsequently by elongation of the colon it assumes a lower position, carrying with it the developing appendix. Occasionally, the fetal situation of the cecum and appendix is observed in later life. Usually in the adult the appendix lies in the right iliac fossa, its base or point of attachment to the cecum being beneath the point described by McBurney and generally known by his name. This point is situated "exactly between an inch and a half and two inches from the anterior spinous process of the ileum in a straight line drawn from that process to the umbilicus." The attachment of the appendix to the cecum varies considerably. In the majority of cases, or according to Treves, in 90 per cent., a medioposterior position is discovered. Frequently the point of attachment is at the lower portion of the cecum on the anterior or posterior surface, or on the outer or right surface.

To some extent the position assumed by the whole appendix is determined by its point of attachment. The position, according to Kelly and Hurdon, is as follows: Horizontally, toward promontory or pointing laterally, 32 per cent.; oblique, toward spleen, 10 per cent.; ascending, 34 per cent.; descending, 24 per cent.

The direction is determined not alone by the point of attachment, but also by the length and character of the meso-appendix, as well as by the size and character of the appendix itself. It is of clinical

<sup>1</sup> *Annals of Surgery*, June, 1907.



importance that the appendix not rarely occupies a position posterior to the cecum and colon (in the retrocolic fossa). It is also important to recall that the appendix frequently extends down into the pelvis, and may be attached by its tip to pelvic structures.

**Meso-appendix.**—The mesentery of the appendix is a triangular or quadrilateral fold of the peritoneum arising from the under layer of the mesentery of the ileum and attached by its right border of the cecum and by its inferior margin to the appendix itself, usually extending about two-thirds the length of that organ from the cecum toward the free tip. The left border of the meso-appendix is free and semilunar or concave in outline. The shape of the mesentery varies to a great extent in different cases, and determines very largely the position of the appendix. Especially important in this direction is the length of its left or free border. The bloodvessels and nerves of the appendix traverse its mesentery, and there may be contained within this structure variable quantities of fat. Occasionally a lymphatic gland (Clado) is found near the root of the meso-appendix.

Considerable variation may be encountered in the shape and position of the meso-appendix, and these variations may determine certain peculiarities in the clinical manifestations of appendicitis. An extension of a serous fold from the appendix to the ovary (appendiculo-ovarian ligament of Clado) is of possible etiological importance. It is supposed to carry bloodvessels and lymphatics, which establish a communication between the circulations of the appendix and ovary. This vascular connection has been denied by some observers (Kelly and Hurdon).

**Coats of the Appendix.**—These are four in number: (1) The peritoneal or serous; (2) the muscular, including an external longitudinal and an internal circular coat; (3) the submucous; and (4) the mucous.

*The Serous Coat.*—The peritoneal layer is a rather firm membrane closely applied to the outer muscular coat excepting along the mesenteric attachment. Occasionally, also, on the side of the appendix opposite the attached mesentery, the serous coat is raised as a fold extending for some distance along the length of the organ. The superficial bloodvessels, lymphatics, and nerves of the appendix lie in a looser subserous tissue. Normally the bloodvessels can be easily seen beneath the peritoneal coat, and when congestion occurs their injection is striking.

*The longitudinal muscular coat* is a continuation of the muscular bands of the large intestine. This connection is of considerable practical importance, particularly as the anterior longitudinal band of the colon and cecum is a direct guide to the root of the appendix. Contractions of the longitudinal coat may considerably shorten the appendix.

*The circular muscular coat*, somewhat less in diameter than the longitudinal, encircles the appendix, but according to Lockwood is deficient at the attachment of the meso-appendix (*hiatus*). This gap transmits vessels, nerves, and lymphatics from the interior to the serous coat.

*The submucous coat* is of variable thickness from 0.2 to 0.8 mm., and is composed of loose connective tissue containing wide lymph spaces, lymphatics, and veins. It is separated from the mucous membrane by

a thin muscularis mucosa. The submucosa contains a considerable amount of elastic tissue, and the lymphadenoid tissue of the mucosa extends well into the submucosa in places.

*The mucous coat* is a redundant mucous membrane presenting on transverse section a folded appearance and having a thickness of about 0.75 mm. On transverse section it is found to contain normal tubular glands or crypts of Lieberkühn and lymphatic follicles lying between the glands and extending from beneath the surface epithelium to and into the submucosa. The surface epithelium is of columnar form, and many of the cells are of the goblet type.

**Circulation.**—The arterial supply is derived mostly from the posterior ileocecal artery. The vessels supplying the appendix traverse the meso-appendix, running toward the tip of the organ distributing branches at various intervals. After reaching the appendix, according to Lockwood, they divide into external branches, which supply the serous coat and the muscular tunics, and internal branches which, penetrating the muscular hiatuses, terminate in branches supplying the mucosa and submucosa. The veins accompany the arteries and terminate in the ileocolic and eventually discharge into the superior mesenteric vein. The return circulation, therefore, extends to the portal system. To a slight extent some communication is established with the systemic circulation through the external colic veins.

The lymphatic circulation is of great clinical importance. The capillaries begin under the epithelium of the mucosa and beneath the lymphatic follicles, and extending from the submucosa pass through the muscular coats to the peritoneal surface, where they terminate in large trunks accompanying the bloodvessels. They usually extend to the lymphatic glands lying posterior to the cecum, and eventually pass onward to the mesenteric glands along the inner side of the colon. Reference has been made to the small lymphatic gland described by Clado, situated in the base of the meso-appendix close to its attachment with the ileum and cecum. In cases of appendicitis, lymphatic glands in other situations have been sometimes found enlarged, such as those along the external or common iliac vessels, and on this account other lymphatic connections have been assumed to exist. It is not improbable, however, that such enlargements of neighboring lymphatic glands may be the result of diffusion of soluble products of infection, independent of the regular lymphatic channels.

**Nerve Supply.**—The nerves are derived from the superior mesenteric plexus and terminate in a plexus of Auerbach and a plexus of Meissner comparable to those met with in other portions of the intestinal tract. Through the solar plexus the nervous mechanism of the appendix is connected with the cerebrospinal system and with the right vagus.

**Etiology.**—Among the causes of appendicitis we may recognize those which are general and those which are determinative. The disease is distinctly one of early life, as is shown by all tables of statistics. The majority of cases occur from the eleventh to the thirtieth year inclusive. Between thirty-one and forty a fair proportion occur, while after forty years the disease rapidly diminishes in frequency, being rarely met

with in the aged. It occurs in the first decennium of life in a small number of cases, and has even been recognized as a prenatal disease.

*Sex* plays a certain part, as the disease occurs in males two or three times more frequently than in females, according to all observers. Some speculation has been indulged in to explain the relatively greater frequency in males, but no satisfactory explanation has been reached. Some authors have believed that the additional blood supply obtained in females through the appendiculo-ovarian ligament prevents obliteration of the circulation, thus obviating an important cause of the disease.

*Occupation* is of no special importance, although it has sometimes been claimed that those whose occupation leads to irregularities in eating and to exposure are more liable to the disease than are others.

*Nationality* probably plays little part. A number of writers have pointed out the comparative rarity of the disease in the negro.

*Heredity* is of no special consequence, although families have occasionally been described in which repeated cases have occurred. In this connection the possibility of simulation must be remembered.

*Digestive disturbances* are perhaps important in a general way, and have often a direct bearing upon the occurrence of the disease. Doubtless chronic gastric disorders may occasion catarrhal conditions of the bowel and favor the development of appendicular infections. A more direct and local relation of gastro-intestinal disease to involvement of the appendix operates in cases in which the cecum becomes distended.

**Local Conditions.**—Among these, various anatomical conditions require consideration. The appendix normally opens by a relatively narrow mouth, guarded by a reflection of the mucous membrane of the cecum known as the valve of Gerlach. In some instances the valve is wanting or the mouth of the appendix is larger than usual, so that the intestinal contents readily find access to the organ, and may be retained in consequence of narrowing lower down or of weakness in the musculature of the walls. In other instances the mouth, or opening, is contracted, and such contents as gain entrance to the lumen of the appendix in a fluid state may be retained after undergoing inspissation or solidification by the admixture of mucus, epithelial cells, and bacteria, so as to form hardened masses or concretions. In still other cases the arrangement of the meso-appendix or abnormal bands of adhesions that surround the organ at some part of its length, or stenoses and angulations, may similarly prove the cause of retention of material within the lumen. Sometimes such constricting conditions are so disposed that, while ordinarily of little effect in the direction of obstructing the discharge of the contents of the appendix, they may become wholly obstructive when the cecum or other neighboring part of the intestine is distended.

Whatever the cause of the obstruction, the result of retention of material is, according to some authorities, a rapid multiplication of the bacteria contained and possibly, also, an increase in their virulence. This may occasion an infection of the mucous membrane and the subsequent changes that have been described as characteristic of the disease.

There can be little doubt that conditions that obstruct the lumen of the appendix at any part of its course are a frequent and potent cause



of inflammations of the organ. Not rarely cases are met with in which the distal end, or half, of the appendix alone is involved, while the proximal portion, separated from the former by some obstructing band, angulation, or stenosis, is uninvolved. Cases are met with in which repeated attacks of moderate severity have occurred, with digestive disturbance and distension of the cecum and colon, and in which the occasion of the appendicular involvement appears to be a temporary increase of angulation and retention of contents, without extensive infection or involvement of the mucosa and other coats. After a repetition of such attacks, a more severe involvement may occur; and the obstructed distal portion may undergo rapid necrosis or gangrene.

**Fecal Concretions.**—They do not of necessity occasion any inflammatory change, although always a menace, and their relation to appendicitis is, in many cases, a very direct one. Concretions are formed by the inspissation of fecal matter retained in the appendix and by the admixture of mucus, desquamated and exudative cells, and multiplying bacteria. According to some investigators, the concretions are always the result of bacterial growth. They are mainly composed of fecal material, with mineral salts, such as phosphate and carbonate of lime and magnesia, and mucus. Not rarely they are stratified in much the same way as gallstones. Such concretions are met with in a relatively large proportion of cases of appendicitis. Deaver found them in about 16 per cent. of his cases; Treves states that they occur in about 30 per cent. of cases; and in some other series the proportions have been even greater. According to Ribbert, they occurred in 38 of 400 appendices.

**Foreign Bodies.**—Various bodies, such as pins, small nails, portions of bone, seeds, and fruit pips, as well as other insoluble substances, may find their way into the appendix, and are occasionally met with in cases of appendicitis. Not rarely parasites have been found, such as *Trichiurus trichiura*, *Oxyuris vermicularis*, and *Ascaris lumbricoides*.

**Effects of Concretions and Foreign Bodies.**—Although concretions may be met with in appendices that show but little, if any, evidence of inflammatory change, it must be considered that they are a potent cause of inflammatory conditions. In the first place, they are capable, through the direct pressure exerted upon the mucous membrane, of causing destructive changes in the epithelium, and thus opening the way for the invasion of microorganisms. This pressure effect is most likely to occur when a concretion has reached a considerable size and when, as the consequence of distension of the cecum or other local conditions, an angulation is produced at the point of lodgement of the concretion. Again, the presence of a concretion may explain the retention of contents within the appendix, and thus may occasion multiplication of bacteria and infection of the mucosa of the obstructed organ. Frequently when gangrenous changes occur in the appendix it is found that the lesions have begun at the point of pressure from a concretion; and when perforation takes place, the opening is opposite the foreign body. In cases of peri-appendicular abscess, the concretions are not rarely found in the abscess cavity, having escaped from the appendix through a perforation. With respect to foreign bodies of other sorts, it is undoubted

that they are capable of exercising irritative and more or less destructive effects upon the mucous membrane and thus of initiating an attack.

**Influence of the Lymphoid Tissue.**—The lymphoid tissue of the appendix is undoubtedly a factor of importance in the occurrence of the intense inflammation of this part of the intestinal tract. Not unlikely, the immunity of the aged to the disease is due to the involution that takes place in the lymphoid tissue, and its more or less complete disappearance in later life. No part of the gastro-intestinal tube is so abundantly supplied with lymphoid tissue except the tonsillar region, and it is noteworthy that these two situations are common seats of intense inflammation in young subjects. Sahli has introduced the phrase “angina of the vermiform appendix,” in recognition of this fact. It is not improbable that the rich supply of lymphoid tissue occasions a local susceptibility to inflammatory conditions.

It is possible, also, that some as yet undiscovered function of the appendix, perhaps of a secretory nature, may play a part in the etiology. It has been shown that lesions of the colon may be caused by the subcutaneous injection into animals of soluble toxic bodies derived from cultures of dysentery bacilli, and it may be that lesions of the appendix may result from the excretion through its mucous membrane of poisons generated by bacterial activity elsewhere in the gastro-intestinal tract.

**The Bacteria of Appendicitis.**—The microorganisms met with in cases of appendicitis are varied. By far the most frequent form is the *Bacillus coli communis*. In many cases it has been found in pure culture; but usually some other organism is associated with it. Streptococci or staphylococci may occasionally be found without any associated germs. More commonly, however, they are found with other forms. The *Bacillus lactis aërogenes*, the *Bacillus capsulatus aërogenes*, the *Bacillus pyocyaneus*, the influenza bacillus, the bacillus of Friedländer, and a variety of others, have been found alone or in various combinations. In the majority of cases appendicitis probably represents a mixed infection, the most important organisms being the *Bacillus coli communis*, the *Streptococcus pyogenes*, and the anaërobic forms. Some observations make it seem probable that the milder cases with localized peritonitis and relatively benign symptoms are principally due to colon infection, while the more intense cases are of streptococcic or anërobic nature.

**Pathology.**—Various terms have been employed to designate what are sometimes described as different forms of appendicitis, such as simple, catarrhal, perforative, gangrenous, interstitial, obliterative. While these terms are applicable to different stages, they are undesirable if they convey an impression that they refer to different kinds of disease. In addition to this objection, it has been pointed out that unfortunate results have occurred from the impression that mild or moderate symptoms indicated a milder form of disease, such as would be suggested by the terms simple or catarrhal, whereas, in truth, the most serious pathological states of the organ may be present when symptoms have been practically wanting.

The beginning lesion may be assumed to be practically always in the mucosa itself, and in the great majority of all cases there is found

in the appendix removed at operation merely a catarrhal or an ulcerative condition of the mucous membrane. In the least advanced cases slight changes are observed, such as shallow erosion with some accumulation of mucopurulent exudate and congestion of the small vessels in and beneath the mucous membrane. In the more serious grades extensive ulceration of the mucosa will be encountered. At the same time, involvement of the submucosa and of the other tunics may be met with. There may be very pronounced changes in the mucous membrane, with but little visible alteration of the exterior of the organ and but little if any increase in its size. To this form or stage, with its almost exclusive involvement of the mucous membrane, the term *catarrhal* appendicitis is most applicable. Nearly always, however, when the mucosa has been considerably involved, extension to other coats will be found to have taken place. Microscopic examinations show in all stages and grades a tendency to necrosis of the lining epithelium with erosion or ulceration and infiltration of the deeper layers with polymorphonuclear leukocytes. Hyperplasia of the lymph follicles and infiltration with inflammatory cells are regularly present. The lumen of the appendix may become distended with accumulated secretions of a mucopurulent character, and sometimes the exudation becomes hemorrhagic from admixture of blood from the ulcerated surfaces. The accumulation of material within the lumen is favored by obstruction or foreign bodies within the appendix.

In all but the mildest cases the submucosa is involved early; congestion of the vessels and, later, stasis of the blood and thrombosis with oedematous swelling constitute the most conspicuous lesions. In severe cases small or considerable hemorrhages in the submucosa are generally seen. The thrombosis of the vessels may occasion secondary hemorrhagic infarctions of the mucous membrane, and thus advance the process. The swelling and infiltration of the mucous and submucous coats soon occasion a hardening and rigidity of the muscular and serous coats in a direct mechanical way. This is particularly marked when obstructions near the mouth of the organ prevent the discharge of accumulating exudation, and thus occasion distension of the lumen.

Whenever the mucous membrane and submucosa are considerably involved, it is customary to find at least slight disease of the serous membrane. In milder cases a little roughening of the usually smooth and glistening surface is observed, and is found to be due to inflammatory changes in the endothelial cells with beginning fibrinous exudation. The extension of the inflammatory process from the interior of the appendix possibly occurs, as Lockwood has suggested, through the normal gaps in the muscular layer. It thus happens that a considerable degree of peritoneal involvement may occur before the muscular coat is to any great extent involved, except by distension and slight infiltration near the submucous junction. Eventually in many cases the muscularis becomes markedly infiltrated and degenerated, and necrotic changes cause a weakening by destruction of the muscle cells. There is rarely extensive necrosis of the muscularis except when complete occlusion of the circulation through twists, bands, or other forms of obstruction has occurred.



Extensive purulent infection may occasion considerable involvement of the tunics or total gangrene of the organ. In other cases there may be considerable change in the mucosa and submucosa and considerable involvement of the serous coat, with relatively small grades of destructive change in the muscularis. Infiltration with leukocytes and other evidences of inflammatory change between the muscle cells is more usually encountered.

The *contents of the appendix* increase with more or less rapidity and in varying ways, according to the nature of the case. In some instances, with stricture or other complete obstruction of the outlet, an increasing purulent exudate may accumulate within the lumen and cause distension of the walls, eventually forming a pus-containing sac (empyema of the appendix). More often the amount of exudation is less abundant, and there is a tendency to solidification of portions of retained fecal matter with exfoliated epithelium, mucus, and masses of bacteria forming small or large concretions. In many instances there are found within the appendix or within abscesses formed around this organ after perforation hardened fecal concretions evidently of older date.

The effect of increasing accumulation of contents in the lumen upon the walls of the organ is manifested in the obliteration of the folded plicæ of the mucous membrane and the conversion of the lumen from an H-shape to a more or less circular outline. With this stretching of the mucous membrane, there is a flattening of the various structures, follicles, glands, etc., and at the same time a similar effect is produced on the submucosa and outer tunics. In some instances the disease becomes quiescent after this stage.

Obstruction of the lumen of the appendix antedating the attack or the result of inflammatory conditions of its walls has an important etiological relation. Similarly, congenital narrowing of the outlet, acquired changes in the mucous membrane of the cecum involving the mouth of the appendix, or obstructions caused by strictures of the wall of the appendix due to previous attacks or by foreign bodies or fecal accumulations within the lumen play an important part. In all of these conditions retention of the contents may occur, the bacteria multiply and probably gain in virulence, and inflammatory conditions result. In other cases, the mouth of the appendix may be open and its lumen wide enough throughout its entire length to permit of discharge of the contents under ordinary circumstances; but there may be at some point a slight narrowing due to a stricture, a band of adhesion on the outside, a twist or a kink caused by a short mesentery, which may become increased by inflammatory swelling of the distal portion of the organ. As a consequence of this increased obstruction the contents and accumulating exudates are confined to the appendix.

Extensive necrosis and gangrene may occur very rapidly and sometimes with very slight involvement of surrounding parts. Complete occlusion of the organ at some one point, and especially by anatomical conditions or old adhesions, which exercise a constricting effect both on the organ and circulation, and unusual intensity of the microorganisms concerned in the etiology, may be determining factors. The contents

of the appendix are a fetid putrefying mass of mucopus with exfoliated epithelium and other tissue elements and bacteria. The appendix presents the black or grayish and black appearance of necrosis and gangrene, and hemorrhagic extravasation under the serous coat and more or less fibrinous exudation upon the serosa are observed. The organ is friable and may tear upon the slightest manipulation. In many instances spontaneous rupture occurs.

**Involvement of Surrounding Structures.**—The most important local result of appendicitis is peritonitis involving the folds and fossæ in the immediate vicinity of the appendix. In mild cases and when the infective cause is of a relatively low grade of virulence the serous coat of the appendix is covered with a slight deposit of fibrinous exudation. Such localized peritonitis does not of necessity indicate actual perforation of the organ with escape of infective material, but may occur from invasion of the organisms into the peritoneal coat through the muscular tunics. The peritoneal inflammation may extend to surrounding parts, and a more or less firm agglutination may take place. The process may advance no farther and many cases of appendicitis after reaching this stage subside, leaving behind adhesions to adjacent structures. In more intensely infectious cases the exudation is greater, and localized abscess cavities are formed between the appendix and the neighboring coils of intestine or the abdominal and pelvic walls. Minute perforations of the appendix after the formation of preliminary attachment by fibrinous exudate to adjacent parts hasten the formation of abscesses. On the other hand, a perforation of the organ without preliminary adhesion, and especially a sudden extensive perforation, may be followed by a widespread peritonitis with but little tendency to limitation. Doubtless the virulence and nature of the infective cause play a considerable part in the liability to rapid softening and necrosis of some part of the wall of the appendix, and at the same time determine the amount of fibrinous exudation that may be present. In the more virulent purulent infections, destructive effects upon the tissues are more marked and exudation of fibrin less pronounced.

**Peri-appendicular Abscess.**—The situation of abscesses resulting from appendicitis varies according to the position of the appendix and of the adjacent parts of the intestine. In the majority of cases the pus cavity is found between the appendix and the ileum at its attachment to the cecum, between the appendix and the head of the cecum, behind the cecum, or between the appendix and head of the cecum and the right abdominal wall and iliac fossa. Less commonly it may be found in the pelvis, in the retrovesical fossa, or in Douglas' pouch. Extension of the infection to the upper part of the abdominal cavity is usually prevented by the omentum and small intestine. In some instances a long appendix lies posterior to the ascending colon and appendicitis may occasion an abscess at some part of its course behind the colon. The wall of the abscess is formed by the adherent appendix, adjacent intestines, other surrounding structures, and by more or less firm masses of fibrinous exudate. The contained pus is usually of ordinary consistence and frequently of fetid odor.

The abscess may rupture in various directions. Most frequently it breaks through the abdominal wall. Next in order of frequency is perforation into the cecum or other portions of the intestinal canal, into the general peritoneal cavity, into the pleural cavity, or into the bladder or uterus. In rare instances extension and perforation into the gall-bladder or ureter have been described. After such rupture inspissation of the remaining contents may occur and cure result.

*General peritonitis* may result from the rupture of a primary abscess, or more immediately from perforation of the appendix in rapid gangrenous or necrotic types of infection. In some cases without perforation of the appendix virulent organisms may escape through the walls of the organ and occasion a general peritonitis, or after the formation of an abscess extension of the infection may occur without discoverable gross rupture of the abscess wall. In these cases of extensive and spreading generalized peritonitis the pus is apt to be thin and serofibrinous from the beginning, and there is but little formation of fibrinous exudate on the surface of the intestinal coils.

**Remote Lesions.**—Aside from the lesions associated with any form of intense infection, such as myocarditis, infective nephritis, etc., various remote lesions may result from invasion of the infective organisms from the appendix into various surrounding structures. Septic thrombosis of the venules of the appendix is a common occurrence, but fortunately does not frequently extend beyond the smallest branches. In some cases, however, ascending thrombosis takes place and may occasion involvement of the larger mesenteric vessels and the portal vein. In these cases secondary pyemic abscesses of the liver result. Extension may also take place through the retrocolic veins and sometimes through new-formed collateral branches of the systemic circulation, and may occasion secondary abscesses of the lungs.

**Chronic Appendicitis.**—After a severe attack of appendicitis, or more frequently after repeated attacks, changes may occur in the wall of the appendix and in the surrounding structures which have been described as chronic appendicitis. In a certain measure this term is justified, because the adhesions, distortions, and other conditions met with serve to maintain a state of congestion and lasting catarrhal inflammation of the mucous membrane, and perhaps also a slight chronic inflammation of the outer walls of the appendix. It would be more correct, however, to regard the conditions under consideration ordinarily as results of acute appendicitis rather than as a chronic inflammation in the strict sense. In cases of moderately severe non-perforative appendicitis, with formation of a limited amount of fibrinous exudate, adhesions probably frequently result after the acute inflammation has subsided. Even quite intense inflammations of the appendix and neighboring peritoneal folds may resolve, as is indicated by the discovery in many cases of dense fibrous adhesions that must have followed a previous intense attack of appendicitis with localized peritonitis.

Besides the adhesions which are found uniting the appendix to neighboring structures, and which incite to subsequent attacks of appendicitis, the organ itself is frequently found thickened, bent, or otherwise altered



by the preceding acute inflammations. Appendicitis of this description furnishes most of the instances of so-called relapsing appendicitis, the thickened sclerotic walls in a measure protecting against perforation and the complications so commonly met with in more acute types.

**Obliteration.**—This may be the result of previous inflammations, and is thus a form of chronic appendicitis. Some authors insist that obliteration may be purely the result of involution in some instances. In cases of post-inflammatory obliteration, the lumen of the appendix is replaced by a cord of irregularly distributed cells and fibrous connective tissue surrounded by muscle and a serous outer coat. Sometimes areas of atypical disorganized mucous membrane are found, but in cases of complete occlusion all resemblance to the normal structure is lost.

**Symptoms.**—In a great majority of the cases of appendicitis the symptoms of onset and the clinical course are more or less similar and distinctive; so that, as a rule, but little doubt exists in the mind of the physician regarding the nature of the disease. A small minority furnishes a sufficient number of instances of irregular onset and course to give the impression that the features are quite as often puzzling as otherwise.

In typical instances, pain in the abdomen, diffuse at first, and limited to the right iliac region after a greater or lesser duration; rigidity of the abdominal walls, especially on the right side; nausea and perhaps active emesis; constipation; rigors, or definite chills, accompanied with or followed by fever, acceleration of the pulse, and a general feeling of profound illness, characterize the initial symptoms and the stage of fully developed appendicitis. Wide variations are frequently encountered, and the symptomatology may be said to be as variable as that of any other inflammatory condition affecting the internal structures.

**Pain.**—Probably the most frequent symptom is pain, which is rarely absent at any stage. It must not be forgotten, however, that even in intense forms, such as those in which necrosis and gangrene occur, pain may be absent from the beginning to the end of the process. Nearly always the patient suffering with appendicitis is seized with a sudden cramp-like abdominal pain, which at first occupies the central or umbilical portion of the abdomen, and subsequently moves toward the region of the right iliac fossa. There are cases in which, from the beginning, whatever pain is encountered is strictly localized in the right iliac region. In other cases the initial pain is vague and difficult to locate.

The nervous mechanism of the appendix explains to some extent the localization of the pain. The afferent nerves are connected with the solar plexus through the superior mesenteric, and thus a connection is established with the splanchnic and the right vagus. The pain of beginning appendicitis is referred to the mid-abdominal region on account of the distribution of the terminals of the splanchnic system to this area. Not rarely, especially in cases in which the appendix has a position posterior to the cecum, pain in the back and in a region posterior to the liver, and even as high as the right shoulder, may be encountered. When the appendix extends downward toward the pelvis, suprapubic, perineal, and ischiorectal pain may be complained of in the beginning, or after a preliminary period of general or mid-abdominal distress.

After the full development of the disease, pain and tenderness, as a rule, are in the right iliac region. There is often a lack of correspondence of the tenderness with the pain. The most extreme tenderness seems to occur in those cases in which the appendix lies relatively near to the anterior abdominal wall, and especially when it is bound by adhesions to the parietal peritoneum. In cases in which the appendix extends downward toward the pelvis and is attached to the bladder or the rectum, or to other pelvic structures, the degree of pain experienced during defecation, micturition, or digital rectal examination may be excessive. Sometimes the pain is referred to distant parts, such as the thorax, the right thigh, the lumbar region, the back, or the upper portions of the abdomen. The position and attachments of the appendix may, to some extent, determine such referred pains, but this is not invariable.

In the fully developed stage, when pain, previously diffuse, has become localized in the iliac region, the area of involvement is usually limited, and, generally speaking, centres at McBurney's point. The character of the pain varies from a steady ache to a paroxysmal, cramp-like or colic-like condition. Tenderness in the same area is usually, but not necessarily, present.

*Cutaneous hyperalgesia* appears to occur in nearly all primary attacks at some stage except, perhaps, in the most violent acute forms. The cause of the sensory condition is probably the distension of the appendix. It has frequently been noted that the hyperalgesia suddenly subsides when perforation of the appendix has occurred. In non-perforative cases the symptom gradually disappears. It is frequently present in second or subsequent attacks, but is often absent when the original attack has been sufficiently severe to destroy nervous tissue in the wall of the appendix. The area of hyperalgesia centres about McBurney's point, although it is not strictly confined to this region. More properly it may be said to occupy the region of the eleventh dorsal area of Head, a band extending on the right side from the middle line below the umbilicus to the lumbar spine posteriorly. The hyperalgesia is determined by pinching or stroking the skin, beginning outside the suspected area and working toward it.

Tenderness must be distinguished from pain, although the two usually coincide. The degree of tenderness varies, as has been pointed out, with the character of the case and the location of the appendix. Its intensity varies from the mildest grades, in which it can scarcely be determined, to such severe degrees that the lightest touch or even the weight of the bedclothes is intolerable. In these cases, as in all those in which painful sensations are prominent, the position occupied by the patient in bed is quite distinctive. He lies upon his back or lightly inclined to the right side, and flexes the right thigh upon the body so as to relieve tension upon the affected portion of the abdomen.

Intense pain of a peculiar character is found in those cases of acute appendicitis in which intestinal obstruction has occurred as a complication. The violent pathological peristalsis with tonic contraction of the bowel that occurs in this condition occasions intense paroxysms of pain, recurring from time to time with greater or less frequency. In

the beginning these pains may be strictly located near the seat of obstruction; but later they often become generalized.

**Rigidity.**—There may be a generalized rigidity in the early stages, when pain also is of a diffuse or generalized character. Later, when the sensory symptoms have localized themselves in the right iliac region, rigidity also becomes limited in its extent and affects the muscles overlying the inflammatory area. A careful comparison of the abdominal walls on the right and left sides will—in most cases of appendicitis, at least—disclose a slight resistance, if not a definite rigidity, affecting the muscles over the diseased area. The degree of this depends upon the location of the appendix and the character of the surrounding lesions. When the organ lies anteriorly and in close relation with the abdominal wall, and when inflammation involves the structures between the appendix and the abdominal wall, the greatest degree of rigidity as well as of tenderness may be expected. There are, however, instances in which, notwithstanding an immediate relation of a diseased appendix with the abdominal wall, muscular rigidity is totally absent. When the appendix lies posterior to the cecum some spasm of the lumbar group of muscles on the right side may occur.

**Reflex Symptoms.**—Those affecting the stomach and the bowel are of greatest frequency and significance. Nearly always, in typical cases, nausea occurs. This may be attended with vomiting at the onset, or some time later, and repeated vomiting may take place. Not rarely nausea occurs without vomiting, and may persist until the disease is well developed. Sometimes repeated vomiting may be a very conspicuous feature and may overshadow pain, tenderness, rigidity, and other symptoms usually more distinctive. The character of the vomiting in the early stages is not peculiar. The contents of the stomach are ejected, with perhaps some bile. Intense, uncontrollable vomiting may terminate in stercoraceous discharges; but this is more usually the result of complicating conditions occurring in the later stages.

**Constipation** is usually a symptom of importance, although not invariably present. In the beginning its cause is found in the reflex nervous influences occasioned by intense pain. Later, inflammatory conditions in the right iliac fossa are mainly operative by causing a local paresis of coils of intestine involved in the inflammatory area, coöperating with nervous inhibition due to pain. In the final stages, when diffuse or generalized peritonitis has occurred, constipation may be the result of a general paralytic condition of the bowels. Various local conditions connected with appendicitis may operate in a purely mechanical way. Thus adhesions between the appendix and the small or large bowel may produce obstruction; or large abscesses may compress and practically obliterate the lumen of the bowel. In some instances there is at first no disturbance in the action of the bowel, one or more normal movements occurring after the onset. In some cases a diarrhoeal condition may exist for a time, but such cases are rare.

**Symptoms of Infection.**—These usually occur, although there are cases in which, despite the existence of a definite infective lesion, generalized symptoms fail to make their appearance. Rigors and chills occur at the



onset of many cases. Sometimes these are pronounced and repeated from time to time.

*Fever* usually appears, although it must be recognized as a symptom of uncertain value. In many cases, in spite of the seriousness of the local lesions, the temperature remains low, while in other conditions simulating this disease fever is of at least as great frequency as in ordinary attacks of appendicitis. In the average cases the temperature soon rises after the onset, being as high as 100° to 102° F. within a few hours. Subsequently, a variable temperature is apt to mark the course. Often the temperature falls to the normal soon after the onset, without reference to the character of the local lesions. Sometimes a continued fever may be present for several days, and may terminate in an irregular fever when peri-appendicular inflammation or abscess has developed. In most instances fever is an uncertain indication; the severest forms of appendicitis may be unaccompanied by elevation of temperature.

Occasionally subnormal temperatures are encountered, and are usually significant of rather intense infections. On the other hand, extremely high temperatures may occur in severe infections with marked local reaction. Even extensive peritonitis may be unattended with elevated temperature. In the later stages, when localized abscesses have formed, irregular movements of the temperature curve are usual but by no means invariable.

The *pulse* indicates the general condition of infection with somewhat more reliability than does the temperature. In many cases in which fever has been absent, rapidity of the pulse has, from the beginning, indicated the existence of a serious lesion. The character of the pulse varies with the nature of the infection and the local conditions. Acute inflammatory lesions with marked reaction are usually attended with a rapid but relatively full and tense pulse. On the other hand, infections extending to the peritoneum, and especially diffuse peritoneal involvements, are accompanied by increasing rapidity of the pulse, often with irregularity and loss of quality. Less intense peritoneal involvement sometimes affects the quality of the pulse in a different manner. In such cases a hard or wiry pulse of moderate rapidity and without any irregularity may be met with. Increasing rapidity of the pulse, loss of quality, and the occurrence of irregularity are grave indications.

*Chills* are sometimes met with at the onset or at various times throughout the course. A considerable proportion of cases begin with rigors or a sense of general coldness, after which nausea and the other symptoms set in. The chills usually cease after the disease has been fairly established, and there is no tendency to recurrence until extension of the infective process has caused invasion of the peritoneum. In peri-appendicular abscess, regularly or irregularly recurrent chills may continue for a long time. Still more marked is the tendency to chills accompanying widespread infection, as in instances of pylephlebitis.

*Leukocytosis*.—The condition of the blood is usually significant of an infective inflammatory lesion. In the great majority of the cases of appendicitis there is a definite leukocytosis, the number of leukocytes usually exceeding 12,000 to 15,000 per cmm. The differential count

shows a marked preponderance of the polymorphonuclear elements. Sometimes the proportion of these forms may reach extreme grades, such as 90 to 95 per cent. When localized peritonitis has developed, the leukocytosis may be increased to even greater figures; but a spreading peritonitis with intense general infection is apt to declare itself by a falling leukocyte count after a preliminary leukocytosis. An increased number of the leukocytes is not, however, invariably present and even in cases of abscess formation the leukocyte count may be normal or subnormal. Such cases are rare, although there are a considerable number of reported instances. It has been maintained by some that a preponderance of polymorphonuclear elements without an actual numerical leukocytosis may occur in appendicitis. Such a condition of affairs is at least rare, and its significance may be questioned.

**Physical Signs.**—Among the objective manifestations of appendicitis those which attend the earliest stages are of the greatest importance, as prompt diagnosis is most essential to proper treatment. Rigidity is undoubtedly a sign of extreme value. Somewhat later than this other objective evidences may be found, among which tumor and abdominal distension are most significant.

**Tumor.**—At the time of the primary rigidity a certain fulness in the right iliac fossa is usually detected. In part, this is the result of the rigid condition of the rectus muscle, which opposes a certain resistance to the palpating hand; and this gives the impression of a mass. If the tenderness is not too great, this rigidity may be overcome and the suggestion of a mass disappears. Very frequently, however, there will be found below the rectus muscle a rounded and somewhat yielding tumor-like resistance, caused by gaseous distension of the caput coli. The nature of this mass may usually be detected by percussion over it, when the tympany discloses the fact that the mass is an air-containing one. The percussion note, however, is not so purely tympanitic as that found on the opposite side, over the sigmoid flexure; probably on account of the thickening by congestion of the surrounding bowel walls and perhaps also the rigidity of the abdominal muscles.

In the later stages, when a peri-appendicular abscess has formed, this may be readily detected as a more or less resilient swelling, or sometimes as a firm mass, without any discoverable indication of fluctuation; but the character of the tumor differs mainly in consequence of its varying situation. When placed anteriorly to the appendix and cecum, extreme tenderness to touch usually renders palpation more difficult and uncertain in its results; but, at the same time, more frequently enables the examiner to determine the existence of fluctuation, as well as the suggestive dusky discoloration of the skin and the subcutaneous œdema. Abscesses on the inner side and posterior to the cecum and appendix cannot be felt so readily, usually cause less superficial tenderness, and are more likely to give the impression of considerable hardness. Not rarely it is difficult to distinguish such from solid growths by palpation alone. Abscesses extending downward toward the pelvis may be so deeply situated as to escape detection through the abdominal wall, but may be felt, upon vaginal or rectal examination, as resistant, elastic,

or boggy swellings to the right of the vaginal or rectal wall. The size of peri-appendicular abscesses varies greatly, the majority not exceeding the size of a lemon or an orange before rupture takes place. Sometimes, however, masses considerably greater than this are encountered, and may by their very magnitude prove deceptive. When external pointing takes place, the appearances are those usual in deep-seated collections of pus that have burrowed and reached the surface.

*The Appendix May Sometimes be Palpable.*—Some authors have claimed that this is frequently the case. Most writers, however, agree that a positive recognition of the enlarged or diseased appendix is seldom possible. In exceptional cases it is exceedingly easy to feel some portion of the appendix or a large part of it. It is not difficult to be deceived and to mistake inflammatory exudates, distended coils of intestine, etc., for the appendix itself. Occasionally, when the appendix is attached to the anterior abdominal wall, the attached portion may be felt as a mass that seems surprisingly near the surface. In other cases the tip of the appendix has been felt high up on the right side of the rectum. More commonly masses here palpated are peri-appendiceal abscesses.

**Abdominal Distension.**—Distension of the intestines is usually an early symptom, and sometimes increases with great rapidity. Reference has been made to the fact that the caput coli is often slightly dilated in the beginning. At the same time, slight general meteorism may be observed. In later stages, increasing distension may take place from one of several causes. If the appendix is ruptured, or if an extension of the infection has occurred through the wall of the unruptured appendix, the result is peritonitis with more or less rapidly increasing tympany. In other cases the distension is the result of obstruction of the lower portion of the ileum, in consequence of violent local inflammation or of ileus resulting from inflammatory or other forms of obstruction. Rapidly increasing general distension occurs in these cases, as in other forms of acute obstruction of the bowel. The absence of distension by no means excludes extensive local inflammation; and even when peritonitis has occurred the abdomen may remain comparatively flat.

**Vesical Symptoms.**—These are frequent. In the beginning there may be pain in the region of the bladder or retention of urine, as the result of nervous reflexes caused by the acuteness of the pain; and retention may persist throughout the whole course of acute cases. As a rule this disappears after the first day. Subsequently, and at times from the beginning, there is, on the contrary, a continuous desire for micturition, especially in those cases in which the appendix extends downward toward the pelvis, and in which pericystitis is present. In such instances the vesical symptoms may completely dominate the clinical picture. Actual cystitis may develop as the result of a direct extension, or in consequence of general infection.

*The urine* frequently presents small quantities of albumin, with a moderate number of hyaline or granular casts. In some instances of greater severity a well-defined infectious nephritis may occur, especially in cases of extensive abscess formation. Albumosuria is of no regularity



of occurrence and of no diagnostic value. In rare instances peri-appendicular abscesses have ruptured into the bladder or ureters.

**General Peritonitis.**—This is the most ominous of the results of acute appendicitis. Unfortunately, this condition may develop very promptly in patients who have presented no symptoms of great gravity; and it is equally unfortunate that it may arise in the late stages after a somewhat benign course. In a small proportion the disease apparently begins with general peritonitis. The onset of the trouble is usually marked by somewhat abrupt indications, significant of rupture of the diseased appendix or of extension of infection to the peritoneum through the unruptured wall. Sharp pain or suddenly increased local tenderness and rigidity, rigors or chills, a rapidly increasing acceleration of the pulse and elevation of temperature, or, in cases of marked infection, a fall of temperature with prostration and symptoms in general significant of shock, are mostly those which indicate the beginning of this grave condition. Soon board-like rigidity of the abdominal muscles, intense tenderness or hyperesthesia over the affected area, sometimes involving the whole abdominal wall, an anxious expression, a hard, small pulse with increasing rapidity, and a dorsal decubitus with a tendency to flexion of the right thigh, are significant of its further extension. Still later, the acute symptoms may ameliorate with the advancing infection and the overwhelming of the system with toxemia. At the same time increasing abdominal distension takes place, and the patient presents the facial and general appearance of one profoundly septic and having spreading abdominal disease. Vomiting may mark the onset, and may continue throughout the course until extreme prostration from septicemia puts an end to this as well as to other acute symptoms.

**Septicemia.**—General septic infection may occur with or without extensive local lesions. As a rule it is most marked in those cases in which the local infective lesion is decided. Irregular chills and high and irregular fever, with a rapid, weak pulse and a tendency to drenching sweats, indicate this complication. Septic symptoms are most marked in those cases in which infective thrombosis extends from the diseased area through the mesenteric into the portal veins, establishing a suppurative pylephlebitis. In these cases, in addition to the evidences of a general septic process, pain is met with in the region of the liver; swelling of the liver may be detected, and jaundice appears. The last-named symptom may occur without pylephlebitis or pyemic abscess, as the consequence of an intense septic infection, but is rarely marked in such instances. Pyemic abscess in other organs, such as the lungs, spleen, kidneys, acute swelling of the parotid gland, and acute infectious nephritis, occasionally occur. Subphrenic abscesses have been encountered in some cases, mainly as a result of extension of cellulitis behind the cecum and colon. Pleurisy may follow or occur independently.

**Clinical Varieties.**—The nature of the process is not essentially different in mild and severe cases, and such terms as "simple appendicitis," "simple catarrhal appendicitis," "gangrenous appendicitis," and the like, are in a certain sense mischievous if they create an impression that there are forms of appendicitis of essentially different character, and

that mild symptoms point to the existence of a benign process, while severe symptoms indicate more serious disease. Practical experience has shown beyond question that the mildest of symptoms may be encountered in cases in which extensive necrosis or gangrene has occurred, while severe symptoms may be met with in cases in which a relatively slight disease of the appendix exists. However much the symptoms and pathological lesions fail to harmonize in certain cases, it cannot be denied that there are many instances of appendicitis in which the mucosa is involved to the practical exclusion of the other parts of the organ. Such cases are, properly speaking, catarrhal appendicitis. Doubtless many such cases occur without clinical symptoms of any sort, in proof of which the experience of the postmortem table might be cited. A second group of cases is that in which all the walls of the appendix are involved, with little or no extension outside; cases in which, in other words, the disease is confined to the appendix itself. A third group is that in which the disease has extended beyond the appendix and has involved the peritoneum or other surrounding structures. Finally, there are cases in which a general peritonitis is associated with appendicitis.

The infective agent may be the same in all of these forms, and the pathological changes do not differ in kind. The different clinical and pathological course is dependent upon varying local conditions affecting the circulation in the appendix and its drainage, and perhaps upon anatomical conditions promoting in some and preventing in other cases rapid extension of the infective process.

**Lesions Limited to the Interior of the Appendix.**—There are cases of simple catarrhal appendicitis in which sudden abdominal pain, at first somewhat general, later limited to the right iliac fossa, slight tenderness and rigidity in the same regions, chilliness followed by slight fever and acceleration of the pulse, a little nausea and perhaps an attack of vomiting and constipation, make up the clinical picture. Sometimes, indeed, little beyond pain and tenderness occurs. After a variable period extending from a few hours to twenty-four or thirty-six hours the symptoms subside, leaving a variable degree of soreness that may persist for several days longer. The subsidence of symptoms is often coincident with evacuation of the bowels. Many such cases are instances of merely catarrhal inflammation, and the pathological lesions are often confined to the mucosa or mucosa and submucosa. The contents of the appendix consist of a scanty viscid mucus mixed with some soft fecal matter and bacteria. At times, when some interference with the drainage of the appendix exists, the contents may be more abundant and composed of inspissated fecal matter with mucus and cellular exudates.

Formerly cases of this sort, in which sudden abdominal pain and tenderness are the principal symptoms, were described by some as cases of "appendicular colic," especially when fever and other manifest indications of inflammation were wanting. At the present time there seems little reason for believing that cases presenting the symptoms indicated are other than actual appendicitis, and even the possibility of a colic of this description arising in an uninfamed appendix must be doubted. Nor is it certain that the colicky pains of actual appendicitis

are even due in large measure to peristaltic efforts on the part of the muscular layers of the appendix.

Unfortunately, the pathological conditions are not always as limited as have been described in cases presenting the symptoms indicated. There may be, with symptoms no more intense than these and with no greater duration so far as can be discovered, extensive necrosis or gangrene of the appendix and the presence of fecal concretions. Indeed, there is every reason to believe that appendicitis of the greatest gravity may be entirely latent, the first symptom appearing when perforation and peritonitis have occurred.

**Involvement of the Whole Thickness of the Organ.**—In cases in which a rapid extension of infection causes almost immediate involvement of the entire wall of the appendix the symptoms are usually more intense, the initial rigor or nausea more pronounced, the fever higher, the local symptoms more pronounced, and, in general, the patient's condition seems more serious. If subsidence of the symptoms occurs, this is more gradual and the local tenderness and rigidity are more prolonged. In the simpler cases there is often a temporary amelioration of symptoms after free evacuation of the bowels, even though the purgation has no permanent good effect. Such relief is much less likely in the cases of extensive involvement of the walls than in cases of the catarrhal type. Associated involvement of the serous covering adds to the gravity, and in a considerable proportion is followed by a localized peritonitis.

**Involvement of Surrounding Structures.**—In some instances, after an acute onset, moderate symptoms may continue for a period of from one to three or even five days, when an exacerbation sets in and evidences of extension of the infection present themselves. In these cases the local symptoms, as well as the fever, nausea, and vomiting, subside, and a few evacuations of the bowels may add to the apparent improvement. Gradually, however, or sometimes quite suddenly, a renewed chill or vomiting and the reappearance of sharp pain initiate the extension to the peri-appendicular structures. Such cases are probably in most instances caused by organisms of relatively low virulence, and occur in individuals whose general or local conditions offer considerable resistance. Unfortunately, however, the sequence of events is often far from being as satisfactory as this. In many instances there is a rapid extension with constantly increasing symptoms, and considerable localized peritonitis develops before any adequate amount of exudate can form to limit the spread of the infection by causing adhesions. After spreading to a certain distance, however, further extension may be prevented by exudation and agglutination of the bowels. In this manner general peritonitis may be prevented, and eventually a peri-appendicular abscess of considerable size may be formed. The symptoms significant of such extensions are usually quite marked, consisting of increasing local tenderness, rigidity, and swelling, increased but often irregular fever, general meteorism with obstinate constipation, indications of cessation of local peristalsis, and finally increased vomiting, perhaps, becoming stercoraceous in character.

In many cases the involvement of surrounding structures occurs



suddenly after perforation of the wall of the appendix. Time of rupture may be indicated by an attack of renewed and severe pain, by a sudden feeling of sinking or prostration, nausea or vomiting, or fall of temperature and acceleration and arrhythmia of the pulse. In other cases no special symptoms occur, but the general features take on an aspect of greater gravity and the local symptoms become more marked. Soon the indications of a circumscribed or general peritonitis appear.

**Chronic Appendicitis.**—Two types may be recognized. The first is one in which, as the result of a previous acute attack, general thickening of the walls of the appendix has remained, or a narrowing of the outlet, an angulation, or some other condition interfering with proper drainage. In these cases local or general abdominal symptoms may be more or less continuously present. In the second group, as a result of shortening or abnormal attachments of the meso-appendix, or in consequence of angulations or adhesions, the appendix, although ordinarily free from inflammatory conditions, is prone from time to time to suffer when sluggishness of the bowels, gaseous distension of the cecum, and especially fecal accumulations in the caput coli or cecum occasion increased tension upon the appendix, increased angulation, etc. Under these abnormal conditions frequent mild acute attacks may occur, and may be quickly relieved by free evacuation of the bowel or correction of the other conditions named. With each recurring attack, however, the appendix tends to become more distorted and damaged, and eventually a violent acute attack may terminate the condition with all the manifestations of a severe acute appendicitis. It is this form to which the term *relapsing appendicitis* has been particularly applied. While this name is used especially to designate cases in which acute appendicitis is supposed to occur from time to time in a relapsing manner, and without any special local condition persisting between the attacks, it is important to recognize that the type above described is probably equally common, or more common, namely, that in which recurring attacks of increased tension or angulation take place without necessarily marked inflammatory conditions, until more severe lesions of the organ are finally established.

In chronic appendicitis of the first type, due to general thickening, adhesions, etc., persistent local soreness, increased from time to time when distension of the bowels occurs, a tendency to more or less troublesome constipation, sometimes an associated mucous or membranous colitis, and evidences of intestinal indigestion, with furred tongue, disturbed appetite, nausea, tympanitic distension, and vague generalized abdominal pains, are met with. Not infrequently attacks of severe cramps or colic may occur when the intestines are particularly sluggish.

In the *relapsing type* attacks occur indistinguishable from those of acute appendicitis, arising without any previous history of involvement of this region. In other cases there are, occasionally, short seizures in which intense localized pain and tenderness, with perhaps slight muscular rigidity, make their appearance without much fever, disturbance of the pulse, or constitutional disorder. When the attacks subside, the return to normal conditions is often so rapid that the thought of a severe local inflammation can hardly be entertained; and an examination of

the blood in these cases usually reveals but little, if any, leukocytosis. It is frequently observed that the acute attack follows some very definite derangement of digestion; and the association of the latter, with the consequent localization of symptoms in the epigastrium or upper portions of the abdomen, and the presence of symptoms suggesting "biliousness," may readily lead to an overlooking of the appendicular disease.

The outcome of chronic appendicitis may be the development of a chronic intestinal disorder, such as membranous or mucous colitis or habitual constipation. In cases of the recurrent type there may be a subsidence of the attacks after several have occurred, and even after attacks of intense violence. There is always, however, the danger that finally a very severe condition may develop; perforation or extension of inflammation to the peritoneum may occur; and the disease may terminate as do instances of violent primary appendicitis.

**Diagnosis.**—The symptoms of acute appendicitis, when marked, are so typical that a diagnosis can scarcely fail to be made. There are, however, many instances of obscure and even of latent appendicitis, in which no amount of clinical acumen or painstaking care will enable the practitioner to determine correctly the nature of the patient's disease, although suspicion may attach to the appendix. On the other hand there is unfortunately a tendency that sometimes makes itself manifest to regard every form of abdominal pain as appendicitis, unless the evidence clearly points to some other disease. However common appendicitis is and however important its early recognition, it would be a misfortune if physicians generally disregarded all that has been learned respecting the diagnosis of this disease by its symptoms, the physical signs, and the clinical examinations, to such an extent as to suspect its presence in all cases of abdominal pain, unless clear evidence of something else were at hand.

The development of sudden pain in the abdomen, followed by a localization in the right iliac region, and attended with rigidity of the muscles over this part, must be looked upon as having great significance. If, in addition, there has been a primary rigor, or nausea and vomiting, with constipation, the diagnosis becomes fairly assured. Fever is a symptom of little importance, and rapidity of the pulse, although a little more trustworthy as an indication, is not necessarily met with. When the pain becomes sharply localized in McBurney's point, and muscular rigidity is found in the same area, the diagnosis is practically established. The existence of leukocytosis is often an aid in differentiating between appendicitis and other affections in the same region.

**The Diagnosis of the Character and Stage of the Disease.**—Attention has been called to the fact that it is often impossible to distinguish between mild appendicular lesions limited to the inner lining or to the walls of the appendix alone and cases of a severer grade, with beginning or even extensive peri-appendicitis. In many instances, however, a diagnosis of the grade of the disease is possible. Simple catarrhal appendicitis is usually recognized by the mildness of the symptoms, by the tendency to rapid amelioration after evacuation of the bowel, and by the early return to normal condition. In cases, however, in

which the symptoms are of equal moderateness, but tend to persist in spite of purgation, and in which even slight tenderness and fever persist, the probability of a more serious condition must be considered. Cases, too, in which the severity of the constitutional condition of the patient is distinctly out of proportion to the local manifestations may properly be suspected of being due to more intense, and perhaps necrotic or gangrenous, lesions of the appendix. Distinctly marked leukocytosis is an additional indication of severity and of probable peritonitis.

Peri-appendicular infection and the development of abscess may be indicated by the continuous increase of local symptoms and the appearance of tumefaction in the right iliac fossa; or by the recurrence of fever, pain, and rigidity after an interval of quiescence succeeding the initial attack. Sometimes the development of peri-appendicular abscess is so gradual and insidious, and the exudative material and agglutinated coils of intestine so thoroughly walled around the focus of disease, that an abscess of considerable size may develop with relatively no local symptoms; and there may be but little fever and other constitutional reaction. In such instances, leukocytosis may be wanting, even though an abscess of considerable dimensions has formed.

Extensions of the infective inflammation to neighboring veins or lymph channels, causing an ascending suppurative phlebitis of the mesenteric veins, and finally of the portal vein, or a lymphangitis of the retrocecal region, are indicated by evidences of intense toxemia and septicemia and by localized symptoms of marked gravity. In the case of retrocecal inflammation the pain may be confined to the back, and may extend upward toward the posterior aspect of the liver.

The development of a spreading peritonitis is indicated by intense constitutional disturbance. The general appearance of the patient is usually somewhat significant. Increasing local tenderness and swelling, with recurring rigors and elevation of the temperature, and with marked disturbance of the pulse rate, followed by general abdominal distension and a cessation of peristalsis, are among the important indications. Leukocytosis may at first rise to higher levels; but in many instances, especially those of severe infectiousness, the leukocyte count suffers an early fall. This may set in so promptly that, by the time the first examination of the blood can be made, a normal count, or even leukopenia, may be discovered.

**Differential Diagnosis.**—The onset must be distinguished from that of a variety of abdominal conditions, any one of which may bear so puzzling a resemblance as to make a certain diagnosis impossible.

*Painful gastro-intestinal conditions* of various sorts must be distinguished. An attack of simple gastric indigestion or of acute gastritis frequently begins with symptoms like those of appendicitis. As a rule the relation to some indiscretion of diet is more immediate and certain; the localization of the pain is more likely to be in the region of the stomach, and to remain in that place; nausea and vomiting and tenderness in the epigastrium are conspicuous; while fever and leukocytosis are less likely to be found. The latter symptoms, however, may occur, especially in children, and the local symptoms may be referred to lower



parts of the abdomen, particularly when the gastric disturbance has been occasioned by a sluggish condition of the bowels.

Acute, painful affections of the small intestine more frequently bear a striking resemblance, and usually in proportion to the nearness of the approach of the irritative or inflammatory conditions of the lower part of the small intestine. Usually the pain and tenderness are more diffuse, and throughout the attack fail to become limited to the right iliac fossa. Rigidity is more general, when present; and the pains are of a more distinctly generalized colic-like character. Disturbance of the stomach is less marked, and diarrhoea more likely to occur. The condition is less liable to present the rapid development of grave symptoms met with in severe cases of appendicitis, and is less likely to undergo the amelioration after free purgation seen in the mild cases of appendicitis.

Intestinal *colic*, whether due to digestive disturbances or to inflammatory conditions of the intestines, may suggest an attack of appendicitis. (See Acute Enteritis.) The resemblance of lead colic is often very striking, on account of the association of obstinate constipation with the acute abdominal pain. The indications of localized inflammation, however, are wanting, and a careful scrutiny of the history and a consideration of the occupation usually enable the physician to arrive at a satisfactory diagnosis.

Acute *enteritis* due to mineral poisoning, such as lead, mercury, or arsenic, as well as attacks of food poisoning, may simulate appendicitis, like other varieties of gastro-intestinal irritation or inflammation. They are distinguished by the general extensiveness of the abdominal symptoms, the absence of localized tenderness or rigidity, and the prostration. Usually, also, there is more or less, and sometimes intense, diarrhoea.

Acute *colitis* resulting from stagnation of the contents of the large intestine and the accumulation of fecal masses in the cecum, or following exposure to cold or digestive disturbances, may simulate an attack of appendicitis. This is particularly the case when the cecum or the head of the colon is especially involved. In some instances an accurate diagnosis is impossible; and it is certain that in some of the cases the appendix becomes secondarily involved, when it must be obvious that the symptoms would bear even a more puzzling resemblance to those of independent appendicitis. Attacks of typhlitis due to stercoral accumulations usually present a less intense degree of local tenderness and rigidity, and are less acute in onset than appendicitis; but cases have been reported in which the local conditions have been violent, and in which stercoral ulcerations have caused perforation with the secondary development of perityphlitis.

*Typhoid Fever*.—The intestinal conditions in the early stages of typhoid fever may simulate appendicitis. Rigidity of the abdominal walls, marked local tenderness, and tumefaction occur in these cases; while fever and the general constitutional symptoms of the onset resemble those of many cases of appendicitis. The gradual onset after a week or more of indefinite malaise and gradually increasing fever, the complete anorexia, the dilated pupil, and the absence of leukocytosis, may aid in the recognition. Unfortunately, some instances of typhoid fever

with the particular localization of the lesions referred to, come on very abruptly, with marked symptoms closely resembling those of appendicitis. To add to the confusion, there is, in a certain number of cases of typhoid fever, an early involvement of the appendix, with the development of specific typhoid lesions in the lymphoid tissues of that structure.

In a certain number of cases ordinary appendicitis may complicate the onset of typhoid fever. It is not improbable that in these cases the specific lesions as in the cecum and the consequent interference with drainage of the appendix may have an important part. The manifestations are similar to those met with independently of typhoid fever, but it may be said that, as a rule, these cases usually pursue a relatively benign course and become quiescent or are resolved.

*Acute intestinal obstruction* may in the beginning suggest appendicitis. The early development of indications of more or less complete intestinal obstruction with marked distension and without the usual evidences of inflammation found in appendicitis, will aid in the distinction.

*Acute pancreatitis, the rupture of a gastric or duodenal ulcer, and acute peritonitis* following rupture of ulcers of other parts of the intestinal tract, suggest appendicitis in the suddenness of onset, the intense abdominal pain, the tendency to nausea and vomiting, the occurrence of fever, and in the constitutional condition of the patient. The localization of the symptoms and the profound character of the disturbance, especially the speedy development of early collapse, enable one to arrive at a proper diagnosis, in the majority of cases, before the condition has proceeded to its more pronounced grades.

*Pneumonia*.—Not rarely the pain in the early stages is referred to the abdomen, especially in children, and a considerable number of cases have been observed in which the resemblance to appendicitis was so puzzling that operation was undertaken. A careful physical examination will, in most instances, prevent this error; but there are cases in which, owing to the lateness of the appearance of distinct physical signs, the diagnosis of pneumonia may be difficult.

*Malaria*.—Attention has been called to the occasional onset of malaria with abdominal symptoms. In these cases the occurrence of a rigor and sudden fever, with intense abdominal pain, suggests appendicitis. There may even be rigidity and localized tenderness. In some instances the diagnosis has been possible only after an examination of the blood.

*Cholecystitis*.—The pain may be referred to the lower right quadrant of the abdomen, and whatever tenderness is discovered may be most decided in the same region. The symptoms of onset may be practically the same as those of acute appendicitis. On the other hand, in cases of appendicitis, the pain may be referred to the region of the gall-bladder; or, when the appendix lies posterior to the cecum, it may be most marked in the back, posterior to the liver. Difficulty in diagnosis may, therefore, arise from the mistaking of cholecystitis for appendicitis, or the reverse. Usually the location of the pain and other symptoms and the discovery of tenderness and swelling in the region of the gall-bladder or in the right iliac fossa, make a proper diagnosis possible.

When empyema of the gall-bladder has followed a cholecystitis the

tumor or mass may be found in a relatively low position, owing to the gradual increase in the size of the gall-bladder. Pain and tenderness are also situated in a lower position than is usual in the acute stages of cholecystitis. As a rule, however, the mass can be found to have a certain pyriform shape and to be dependent from the under surface of the liver; and the point of maximum pain or tenderness is usually above the transverse umbilical line.

*Biliary colic* simulates appendicitis in the suddenness of its onset, the intensity of the pain, and the associated rigidity of the abdominal muscles, together with nausea and other gastric symptoms. As in other hepatic and biliary conditions, however, the pain is situated higher up; and the development of jaundice is an important distinctive indication. Intense and repeated vomiting is never as frequent in biliary colic as in the average case of appendicitis.

*Biliary cholelithiasis* without definite attacks of biliary colic has often been mistaken for subacute or chronic appendicitis. The frequent occurrence of slight or severe pain in the right half of the abdomen, the pain not rarely being referred to the lower right quadrant, and the tendency to disturbance of the intestinal tract and to more or less gastric disorder, are the suggestive symptoms. Not infrequently, in these cases, an enlargement of the gall-bladder is present. Suggestive tenderness in the region of the gall-bladder is one of the most important symptoms upon which a diagnosis may be made.

*Nephrolithiasis and Renal Colic.*—In acute attacks of renal colic the intense pain radiating from the loin to the external genitalia and disturbances in micturition (temporary obstruction, followed by the appearance of blood-stained urine) are the symptoms of special importance. When a calculus has worked its way to the lower portion of the ureter and has become fixed in this position it may occasion acute attacks which are most difficult to distinguish from appendicitis. The pain and localized tenderness, if the right side is affected, may be in precisely the region of the appendix, and may show less tendency to radiation downward. The character of the pain, however, is often of a distinct cutting nature; disturbances of micturition, the appearance of crystals or blood in the urine, and finally the result of *x-ray* examination, may establish the diagnosis.

*Acute pyelitis and other inflammatory conditions of the kidney* may be attended with considerable pain, and may, therefore, simulate appendicitis. The situation of the pain, the discovery of tenderness in the loin and perhaps enlargement of the kidney, and the results of an examination of the urine, make the diagnosis possible.

*Movable kidney* has frequently been mistaken for appendicitis, the sudden occurrence of painful attacks (Dietl's crises) being the principal occasion of confusion. These attacks may be indistinguishable in their character or location from the cramp-like pains of a beginning appendicitis. A careful physical examination usually makes the diagnosis possible by discovering the more or less movable enlarged kidney. The greatest difficulty occurs in persons in whom the abdominal walls are sufficiently thick to prevent careful palpation, or in whom muscular



rigidity is unusually pronounced. Among the distinguishing symptoms the most important are those arising from disturbance of micturition.

*Acute peritonitis* from various causes other than those before mentioned may simulate appendicitis. Thus tuberculous peritonitis, or peritonitis following perforations of the intestines or other hollow viscera of the abdomen, or consequent upon extension of pelvic infection, may resemble appendicitis superficially and even on most careful examination. Preceding conditions, the location of the symptoms, the early evidence of more or less extensive involvement of the peritoneum, and the absence of the more or less localized involvement of the right iliac region, enable the physician to arrive at a correct diagnosis.

*Salpingitis* and *oöphoritis*, with or without localized peritonitis, may offer considerable difficulty in some instances. In these cases the frequency of pain in the pelvic region and back, the occurrence of other pelvic symptoms, and the location of the acute tenderness, are suggestive indications, while the results of vaginal examination usually give a correct diagnosis. The early development of a localized peritonitis in these cases increases the difficulty of diagnosis, especially when the history of the earlier symptoms cannot be obtained or is uncertain.

*Ovarian Neuralgia*.—In some patients, particularly in neurotic young women, attacks of intense pain in the right lower quadrant of the abdomen may occur at the beginning of menstruation, and may persist through the whole period. Sometimes these seem to be dependent upon overloading of the cecum, when a certain fulness will be detected on palpation. Moderate fever occasionally occurs. The resemblance to acute appendicitis may be very puzzling especially when, as a result of apprehensiveness, nervous mimicry of other symptoms, such as gastric disturbances and muscular rigidity, occur. A careful study of the general condition, the absence of leukocytosis and of a characteristic clinical course, may establish the diagnosis; but in some cases doubt must remain even after subsidence of the symptoms at the end of menstruation.

*Nervous mimicry of appendicitis* may also occur in women at other times and perhaps with nearly equal frequency in neurotic males. It must be remembered that there is a certain degree of physiological sensitiveness at the ileocecal valve which may readily increase under nervous conditions, and abdominal rigidity is not infrequently met with under the same circumstances. The general indications of infection and local inflammation, however, are wanting, and if the nervous character of the patient is recognized a proper diagnosis is usually easy.

**Prognosis.**—Although the majority of patients with acute appendicitis recover, the disease must be regarded as one of decided seriousness, because it is often impossible to determine that an unfavorable extension, which may terminate in rapidly fatal peritonitis, is about to take place; and because, in cases of recovery, such after-results remain that recurrent attacks will probably recur.

Treated in a purely medical or tentative manner, the great majority of patients with appendicitis recover. It is impossible to quote figures that may be relied upon to express the exact truth, since it is extremely difficult to recognize milder cases with certainty, and sometimes even

the severest forms would pass undiagnosed but for the character of the terminal conditions. The greatest difficulty is caused by the fact that there is a very large group of cases of extremely mild character in which pain, slight gastro-intestinal symptoms, possibly moderate fever, and rigidity in the side may occur, but in which the physician may hesitate to make a diagnosis of appendicitis. Practically all these recover, and very many of them certainly are never classified as instances of appendicitis. The result is that tables of prognosis fail to include at least a large number of instances, and consequently present a less favorable impression than would be the case if all were included. Even with this error, which tends to make the outcome of the disease seem somewhat less favorable than it should be, the recoveries from appendicitis treated by ordinary medical means or by expectant methods constitute a very large proportion of the total number of the cases.

Sabli collected 7213 cases, of which 473 were operated on; while 6740 were not. Of the latter group, 91 per cent. recovered. Recurrences took place in 4593 cases; and of these, 3635 recovered without further recurrences. It must be recognized, in connection with such statistics, that it is probable that the cases in which operation was performed represented a disproportionately large percentage of the serious cases. On the other hand, cases in which the disease had advanced rapidly and operative measures seemed futile would be classified in the group of those not operated on.

A study of the surgical literature convinces one of the fact that the mortality from acute appendicitis treated by prompt and skilful surgical methods is probably lower than that recorded in most of the statistics bearing upon the results obtained from medical or expectant methods. In a measure these statistics may be somewhat deceptive in that they fail to include some of the most serious cases in which operation has been deemed inadvisable, and, on the other hand, include some cases of doubtful diagnosis. Objections of a similar nature might, however, be urged against statistics pointing the other way.

The liability to perityphlitis is always very great. Some instances occur of appendicitis without extension beyond the walls of the organ, but the tendency to extension through the walls or to perforation is extremely great. In those cases in which, as the result of an angulation, bend, adhesion, or other form of stenosis, temporary interference with drainage occurs when the cecum is distended, mild catarrhal attacks may be met with from time to time, without very great liability to extension. Eventually, however, in these a severe attack may occur and may terminate in the usual manner.

The liability to diffuse peritonitis is decidedly less marked than that to perityphlitis. The mode of extension of the infection is such, and the reactive process in the neighboring peritoneum so prompt, that limitation of extension is usually brought about by the agglutination of neighboring coils of intestine and the formation of a restraining wall of more or less firmness. It is unfortunate that no method of diagnosis enables the physician to determine the existence of conditions that may lead to the sudden rupture of an inflamed or a necrotic appendix.

The liability to relapse after recovery from acute appendicitis is very great, although it cannot be accurately estimated in figures. There are many instances of recovery with no subsequent tendency to recurrence, especially in those cases in which a total obliteration occurs. The usual manner of recovery is by the formation of more or less fibrous thickening or adhesion, and such conditions predispose to subsequent reinfection.

**Treatment.**—It is difficult to state in a categorical manner whether this should be invariably surgical, or only in selected instances. Medical men, as well as surgeons, recognizing that it is often impossible to determine when an apparently benign case will terminate in sudden extension or rupture, with the development of peritonitis, believe that it is usually wiser to regard every case of appendicitis as demanding surgical treatment. A few years ago it was urged by many surgeons that every case in which the diagnosis had been established demanded immediate operation, unless some unusual contra-indicating circumstance prohibited that method of treatment. This attitude was supported by statistical evidence that seemed to show that, taken all in all, more cases would recover if all were subjected to immediate operation than if an attempt were made to select those in which operation was desirable and to postpone operation in other cases. However much it may be urged, on the ground of such statistical evidence, that every case of appendicitis should be subjected to immediate operation, nearly all physicians and surgeons of experience do hesitate in certain cases with mild and perhaps doubtful symptoms, and sometimes even in cases of frank although not threatening character, preferring to await the development of more definite evidences or of more imperative indications for operation in the hope that, when the inflammation has become limited or has subsided, the safer interval operation may be performed. Recently, moreover, some surgeons of large experience, as Ochsner, advocate delay in operation in some cases of appendicitis with spreading infection. This view was formerly advocated mainly by European surgeons.

It happens, therefore, in practice that among any series of cases a certain number will be regarded by both the physician and the surgeon as proper cases for non-operative treatment. In other instances the existence of some complication or coincident disease of a prohibitive character may prevent operation; and finally, certain patients positively refuse operation when it is proposed. Leaving out these exceptional cases the only safe plan is immediate or prompt operation.

**Medical Treatment.**—The first appearance of symptoms suggestive of appendicitis demands immediate rest in bed and the utmost possible relaxation of the patient. In many cases the character of the symptoms of onset is such that the administration of a purgative may seem indicated before the symptoms have become marked enough to be more than suggestive. In view of the possibility of an acute appendicitis, the physician should in such instances select gentle measures, so as to avoid any unnecessary violence of peristaltic action. Enemata are more desirable than purgatives; and of the latter, small doses of calomel, or the cautious use of salines administered at short intervals until effective, are preferable to a single large dose of the same remedies or to more



active purgatives. After symptoms definitely indicative of appendicitis have appeared, the use of purgatives, even of the milder sort, requires careful consideration. The present view of most surgeons is opposed to their administration. Perhaps, however, such a generally sweeping rule is unwarranted. There are undoubtedly cases of mild type accompanying constipation and retention of feces or of gas in the cecum and colon in which gentle purgation is both satisfactory and effective. Not rarely, in such instances, the free evacuation of the bowel may reestablish adequate drainage and cut short an attack that might otherwise proceed to a more serious extent.

*Pain* is one of the symptoms that usually requires special consideration when medical treatment is demanded. In the beginning, when the nature of the pain is still somewhat doubtful, warm applications, such as large fomentations, hot-water bags, poultices, or stupes, may relieve pain as well as gastric irritability. When the symptoms have become more localized in the region of the appendix, applications of cold are preferred, because of a possible controlling influence on the inflammation itself, and because they are rather more effective in controlling the pain. Ice-bags, cloths moistened with ice-cold water, ice poultices, etc., may be employed. They may be left in place continuously, or may be applied from time to time, for such periods as the tolerance of the patient will permit.

The use of *opium* has been generally discredited because of its tendency to mask the symptoms and because in case of subsequent operation it so interferes with peristalsis as to complicate seriously postoperative conditions. Sometimes, however, despite theoretical and practical objections, the degree of pain is so great that small doses of opium are demanded when the diagnosis is still in doubt or when operation is contra-indicated. Certain surgeons advocate minimal doses, even in cases in which the diagnosis has been made and operation is contemplated. In no circumstances should this drug be used in large amounts.

Occasionally, when gastric irritability, meteorism, and general intestinal colic are conspicuously associated with the other symptoms, carminatives, such as spirit of chloroform, Hoffmann's anodyne, menthol, oil of peppermint, phenol, etc., may give relief. Excessive gastric irritability may be controlled by small doses of cocaine, phenol, dilute hydrocyanic acid, cerium oxalate, or aromatic spirit of ammonium. In some cases in which operation cannot be performed, or in postoperative gastric distension and distress, lavage will occasionally put an end to troublesome or threatening symptoms.

**Diet.**—In the beginning stages, all food, and even water, should be withheld. If excessive thirst is complained of, small pieces of broken ice may be allowed; or, after evacuation of the lower bowel, enemata of warm water may be given to supply the needs of the system. If acute symptoms have subsided after forty-eight hours, a cautious return to liquid diet may be advisable. Milk or broth, in doses of from a dram to half an ounce, may first be given, and increased as the tolerance of the patient becomes apparent. A return of local symptoms, fever, or gastric disturbance should suggest the immediate withdrawal of food.

**Treatment of Chronic Appendicitis.**—Cases in which a history pointing to one or more previous attacks of appendicitis is obtained, and in which local symptoms and physical signs or disturbances of bowel function indicate the probability of adhesions, thickening, angulations, or other chronic alterations in and about the appendix, must be carefully considered with reference to the desirability of operation in the interval before the occurrence of another acute attack. When the diagnosis is certain, operation should be unhesitatingly recommended; and even if somewhat uncertain, operation is the safer plan when the occupation or life of the patient is liable to take him beyond the reach of immediate surgical aid should another acute attack occur. The risk from operation in the interval is exceedingly small, but the slight danger incident to general anesthesia, the possibility of other accidents in the course of or following the operation, and the danger of postoperative hernia (not to mention the inconvenience, expense, and other undesirable features connected with an unnecessary operation) should prohibit exploratory incisions in cases with doubtful, even though somewhat suggestive, symptoms. It is better to await developments. Operations are sometimes recommended in cases in which obstinate abdominal symptoms of obscure character but not strongly indicative of appendicitis have occurred. Exploration will more likely fail than succeed in revealing any chronic disease of the appendix. In the great majority of cases chronic conditions of the appendix furnish sufficiently clear indications to establish at least a presumptive diagnosis.

### TUBERCULOSIS OF THE APPENDIX

Tuberculosis of the appendix is occasionally met with at operations and at autopsy. It is said to be found in 2 per cent. of the operation cases (Lockwood). The condition is, like other forms of intestinal tuberculosis, usually secondary to tuberculosis of the lungs. It may occur independently of other involvement of the intestines, but is more commonly found in association with tuberculosis of the cecum. In a few instances primary tuberculosis of the appendix has been met with. The lesions are of variable character. Usually there is a simple tuberculous ulceration; in other cases, extensive invasion of the walls of the appendix, with secondary caseation and pus-formation, may be found; while extensions to the peritoneum, in the form of miliary tubercles, or a more diffuse localized peritonitis, may be seen. Crowder has described a case of primary hyperplastic tuberculosis limited to the appendix, and similar to hyperplastic tuberculosis of the cecum (*q. v.*).

**Symptoms.**—These may be indistinguishable from those of ordinary appendicitis; and a large number of the cases that have been reported have been discovered upon surgical operation for supposed appendicitis. In some cases a suspicion of the nature of the process might arise from the fact that there is, at the time, decided enlargement of the regional lymphatic glands. A case of this sort has occurred in the experience of the writer, and the nature of it was readily recognized before operation. In some cases secondary tuberculous abscesses form.

### ACTINOMYCOSIS OF THE APPENDIX

A number of instances of this condition have been reported. Spickenbaum collected 27 cases from the literature (Kelly and Hurdon). The symptoms are those of a sudden or gradually developing lesion in the right iliac fossa, with the development of persistent soreness and a tender swelling. Rarely the process remains limited to the appendix. Usually it tends to spread to the neighboring structures.

### CYSTIC DISTENSION AND MUCOCELE OF THE APPENDIX

Retention cysts of the appendix are not uncommon. They result from the gradual transformation of the contents of the appendix, in cases of obstruction of its mouth or of obstruction of its lumen, into liquid of a serous or watery character. Considerable dilatation of the distal portion of the appendix may occur, and a cyst of sufficient size to be detected through the abdominal walls may be formed. The wall of the appendix suffers attenuation, and sometimes hernial protrusions of the mucous membrane between the separated fibres of muscularis may be seen. In most instances such dropsical cysts have been found at operation or at autopsy, not having been suspected during life. In some cases operations have been undertaken for suspected abdominal or pelvic tumors, and the condition described has been found.

**Mucocele.**—This is a condition in which the appendix is found distended with grayish or whitish gelatinous material of a mucoid character. In some instances this may be the result of an inflammatory condition resulting from occlusion; in other cases the histological features suggest a neoplastic process. In some of these cases the condition was found in association with papillomatous disease of the ovary.

### TUMORS OF THE APPENDIX

**Polyps.**—Rarely polypoid outgrowths from the mucous membrane occur in the appendix as in other situations.

**Myxoma.**—One instance, shown by Churton and removed by Mayo-Robson, is referred to by Kelly and Hurdon.

**Myoma.**—A few instances are described in the literature. Small nodular masses, about 5 mm. in diameter, occurred in the case described by A. O. J. Kelly. There was chronic inflammation of the appendix.

**Malignant Tumors.**—*Primary carcinoma* of the appendix occurs more frequently than is commonly believed. Kelly and Hurdon state that there are now on record 49 cases, including 2 designated as endothelioma. In most instances in which the situation was noted the growth occurred at or near the tip. The tumor is usually small, having been in 15 cases from 5 to 12 mm. in diameter. Larger masses have, however, been reported up to the size of a walnut. The gross appearance may be



that of a fibrous tumor. Sometimes it has presented caseation, and has suggested tuberculosis. Microscopically, the appearances are those of a glandular intestinal carcinoma. Sometimes infiltration as far as the meso-appendix occurs, as in a case reported by Norris; 9 of the 11 cases studied by Kelly were of this description. Carcinoma of the appendix is somewhat peculiar in the early age at which it presents itself. Of 25 instances of primary carcinoma, 4 occurred under twenty years of age, and 11 between twenty and thirty years. The youngest reported case is that of a girl, aged twelve.

The clinical symptoms are practically indistinguishable from those of chronic appendicitis or of appendicitis with perforation. A fatal termination may be due to perforation and secondary peritonitis. Perio- appendiceal abscesses are not uncommon. Extension of the carcinomatous process to surrounding structures occurs in a certain number.

The *prognosis* after removal has not, as yet, been certainly determined, because the time that has elapsed since the first operation for this condition was undertaken is relatively short. Halsted's patient, according to Kelly and Hurdon, was living five years after operation.

*Secondary carcinoma* of the appendix is occasionally met with, especially in association with carcinoma of the pelvic organs.

**Sarcoma.**—Sarcoma has been found in a few instances.

### TUBERCULOSIS OF THE INTESTINE

Intestinal tuberculosis may result from the ingestion of tuberculous meat or milk (primary intestinal tuberculosis), as distinguished from secondary intestinal tuberculosis, which results from an infection of some part of the intestinal tract from a previously existing focus. This is, in most cases, pulmonary tuberculosis, the intestinal lesion usually resulting from the swallowing of bacillus-bearing sputum. Less frequently secondary tuberculous enteritis results from the extension of a tuberculous focus in the peritoneum, the abdominal lymph nodes, or one of the abdominal viscera.

Concerning the relative frequency of primary and secondary intestinal tuberculosis, Zahn<sup>1</sup> places the occurrence of primary intestinal tuberculosis at 2.27 per cent., while Ciechanowski,<sup>2</sup> on the basis of 13,203 autopsies, figures it at 1.04 per cent. Secondary intestinal tuberculosis Zahn found in 63.21 per cent. of cases of pulmonary tuberculosis. In this connection the results of the investigations on the frequency of tuberculosis, especially of the digestive tract, in children dying of diphtheria are interesting. Among 714 cases dying of diphtheria Heller<sup>3</sup> found tuberculosis in 140 (19.6 per cent.), in 53 (7.4 per cent.) of which it was primary in the digestive tract. Councilman, Mallory, and Pearce<sup>4</sup> in 220 cases found tuberculosis in 35 (16 per cent.), in 13 (5.9 per cent.) of which it was primary in the digestive tract. Among

<sup>1</sup> *Münch. med. Wochenschrift*, 1902, Nr. 2, p. 49.

<sup>2</sup> *Wien. klin. Wochenschrift*, 1907, Nr. 37.

<sup>3</sup> *Deutsch. med. Wochenschrift*, 1902, Nr. 39, p. 696.

<sup>4</sup> *Diphtheria*, Boston, 1901.

806 diphtheria cases Baginsky<sup>1</sup> found 144 (17 per cent.) to be tuberculous, and in only 6 (0.7 per cent.) was it primary in the digestive tract.

Although the commonest lesion of intestinal tuberculosis is the tuberculous ulcer, other processes may present themselves either in conjunction with ulceration or independent of it. Certain clinical distinctions may differentiate these cases and make it profitable to consider separately the ulcerative, the stenotic, and the hyperplastic varieties. Clinically, it may be found difficult to classify all cases strictly according to these types, and frequently combinations exist.

**Tuberculous Ulcers.**—The most frequent localization of tuberculous ulcers is in the ileum just above the ileocecal valve. They occur, however, as high up as the duodenum and as low down as the rectum. The ulcer usually begins in a solitary follicle or Peyer's patch, although it may occur in the mucous membrane itself. It commences as a small, shot-like, gray nodule just below the mucous surface. This enlarges and later its centre undergoes caseation. Microscopically it consists of a number of typical tubercles composed of giant cells, epithelioid and lymphoid cells, or of a diffuse caseating mass. Finally, the entire nodule becomes caseous and subsequently breaks through the overlying mucous membrane, the caseous material is discharged into the bowel, and the tuberculous ulcer results. At this stage it has a small, crater-like opening, elevated caseous edges, and a caseous base. Frequently a number of these primary ulcers unite to form a larger ulcer. In other cases the larger ulcers result from the simple increase in size of the single original ulcer, by the caseation of miliary tubercles deposited about its margins. Since this extension is by means of the lymph channels, the longest diameter of the ulcer is usually at right angles to the long axis of the intestine, and at times the ulcer extends as a girdle about the entire lumen of the bowel. The margins are elevated, irregular, and usually slightly undermined. Frequently tubercles can be seen with the naked eye in the elevated thickened edges. The peritoneal coat of the ulcer is usually thickened, of a dark, bluish-gray color, and frequently contains miliary tubercles. At times the peritoneum corresponding to the area of ulceration is covered by a fine exudation that may lead to adhesions between adjacent coils of intestines. The extent to which the ulceration may proceed varies greatly. Usually ulcers of varying size and age will be found in the same case.

**Terminal Changes.**—Complete healing with the disappearance of all tubercles is unusual. The ulcers frequently undergo partial organization, so that while some ulceration remains, a moderate degree of stenosis is also present. Perforation is seldom a complication of tuberculous ulceration, except in the rectum. Two factors tend toward this infrequency: the thickening of the peritoneal covering and the tendency to the formation of peritoneal adhesions. It is consequently especially in young, rapidly progressive ulcers that the tendency to perforation is greatest. If perforation occurs, either a general peritonitis results, or, if adhesions between adjacent coils of intestines have formed, walling

<sup>1</sup> *Deutsche med. Wochenschrift*, 1902; *Vereinsbeilage* Nr. 35, p. 270.

off the seat of perforation, a localized peritoneal abscess results. On account of the fact that the ulcers are most frequent about the ileocecal valve and usually most advanced in this area, the site of the perforation is relatively most frequently found in the right iliac fossa, or in the pelvis where the coils of the lower ileum usually lie. Occasionally multiple perforations have been found. Perforation has been known to occur into neighboring organs, as the bladder or uterus. Ulcers in the rectum not rarely perforate and cause ischiorectal abscesses. Carcinoma has been known to develop in the site of an old tuberculous ulcer.

**Symptoms and Diagnosis.**—The symptoms of ulcerative tuberculous enteritis do not differ materially from those of simple enteritis or of other forms of ulceration of the bowels. The most constant and characteristic symptom is diarrhœa, but this is by no means invariably present even with quite extensive ulceration. The stools are either soft and unformed, although presenting no special alteration from the normal in other respects, or thin and watery. Mucus may be found in small masses, or as strings or shreds, especially in the cases in which the feces are semisolid. There may be admixture of blood in small quantities, and occasionally considerable hemorrhage occurs. When formed stools are passed, or when the feces are hard from constipation, they may be coated with blood-streaked mucus and pus, provided the ulceration is situated in the lower bowel. Continued diarrhœa causes rapid emaciation and loss of strength, although occasionally the patient maintains his flesh and strength surprisingly. Soreness and localized tenderness are not usually marked unless extension to the peritoneum has occurred. Ordinarily the temperature is not much influenced and any fever is usually due to the primary pulmonary lesion.

Since the symptoms do not differ materially from those of most of the chronic inflammatory and ulcerative conditions in the intestines, the *diagnosis* must rest to a great extent on the associated phenomena. Due attention must be paid to the fact that in children primary intestinal tuberculosis is much more common than in adults, and that more than 50 per cent. of the cases of pulmonary tuberculosis in adults are complicated by intestinal ulceration. Consequently the occurrence of diarrhœa and other symptoms of enteritis in an adult suffering from pulmonary tuberculosis would justify strong suspicions of the existence of intestinal ulceration. At the same time amyloid disease of the intestines, the most prominent symptom of which is diarrhœa, is a common complication of tuberculosis. The diarrhœa of amyloid disease is usually more watery than that of tuberculous enteritis, and is less commonly associated with the presence of occult or visible blood.

In children the diagnosis is usually more difficult than in adults. A persistent diarrhœa, with progressive wasting, abdominal pain and distension, and enlarged glands without determinable cause, would warrant a tentative diagnosis of tuberculous enteritis. In both adults and children the diagnosis would be greatly strengthened by the discovery of tubercle bacilli in the stools or a positive tuberculin reaction. When infected sputum is swallowed tubercle bacilli may possibly be found in the feces before an intestinal lesion has occurred.



**Stenosing Tuberculous Enteritis.**—Stenosis of the intestines of tuberculous origin without ulceration results when the tendency to organization as a result of the inflammation exceeds the tendency to destruction of tissue. It is by no means frequent, but probably not so uncommon as has been formerly considered. A distinction must be made between those cases in which stricture has succeeded upon ulceration and those in which the stenosis is the primary and predominating feature. The latter constitutes the type now specially under discussion. The tuberculous nature of these strictures is sometimes determined only with the greatest difficulty. Fibiger reports two such cases which were shown to be tuberculous only after exhaustive microscopic examination. He thinks that in the past many of these cases have been looked upon as syphilitic. The strictures are most frequently found in the ileum and colon and are usually multiple. The symptoms are those of chronic intestinal obstruction, and the tuberculous nature of the condition can be diagnosed only by the associated lesions or by exclusion of other etiological factors. The tuberculin reaction may be of great assistance.

**Chronic Hyperplastic Intestinal Tuberculosis.**—This is characterized pathologically by varying degrees of stenosis and ulceration, but primarily by a proliferation of tuberculous granulation tissue in the intestinal wall. This leads to a great increase in thickness of the wall and consequent stenosis, which produces one of the predominating clinical manifestations. The condition may originate in either the mucosa or the serosa, and is usually secondary to tuberculosis elsewhere. Its almost invariable site is the ileocecal region. The predominance of the hyperplastic over the destructive processes is probably a result of decreased virulence of the tubercle bacillus.

According to Conrath the majority of the cases occur between the ages of twenty and forty years. The active symptoms are preceded by a long duration of vague, rather mild intestinal disturbances. Not until the stenosis is sufficient to produce symptoms of obstruction is the condition possible of diagnosis. These obstructive symptoms are of insidious onset and form one of the most constant features that the condition presents. A tumor presents itself sooner or later, and the resemblance to carcinoma is often marked. Obrastzow looks upon the slow and late development of the stenosis as pointing to tuberculosis rather than to carcinoma. The mass usually has a cylindrical form, giving the impression of a greatly thickened intestinal wall. Occult blood is usually present in the stools, and frequently the feces contain visible quantities of admixed blood. Fever usually occurs. The diagnosis is substantiated by tuberculosis elsewhere, by a positive reaction to tuberculin, or by the discovery of tubercle bacilli in the stools.

**Treatment of Intestinal Tuberculosis.**—The prevention of intestinal infection is to some extent possible. Patients suffering from pulmonary tuberculosis should be made to realize the danger of swallowing sputum. Unfortunately, this occurs during sleep and cannot then be prevented. The main purpose of treatment after ulceration has occurred should be to save the patient's strength by controlling diarrhoea and as far as possible the ulceration itself. There is some tendency toward healing,

but the object is not so much to secure this result as to control the waste of the patient's vitality. Careful regulation of the diet is an essential. This may necessitate some diminution in the amount of food that might otherwise be desirable, but careful consideration is necessary to decide whether it is wisest to limit feeding on account of the bowels or to continue overnutrition on account of the pulmonary and general infection. No set rules can be laid down. Pasteurization or predigestion of the milk is often desirable.

So far as remedies are concerned, it is always well to use those that are least likely to disturb the stomach. Small doses of bismuth subnitrate, subgallate, or salicylate given rather frequently and continued for some time may have a useful effect. Among the antiseptics, guaiacol carbonate, creosote, carbolic acid, ichthyol, or iodoform may be used. When diarrhœa is excessive, small doses of nitrate of silver, acetate of lead, and vegetable astringents may be administered temporarily or until the bowels become more settled. Sulphur seems to exercise a useful effect in some cases. When ulcers are found in the rectum, direct treatment may aid healing and prevent extension to the perirectal tissues.

The stenosing and hyperplastic forms demand surgical treatment if the symptoms are pronounced and the condition of the patient permits of operation. The results in some cases have been very satisfactory.

### SYPHILIS OF THE INTESTINES

Intestinal lesions of syphilis are rare. They occur in both congenital and acquired syphilis but are much more common in the former. The intestinal lesions of congenital syphilis are always associated with syphilitic phenomena in other organs. They usually take the form of multiple small gummata, and are found almost solely in the small intestines, and especially in the ileum. They take the form of flat, grayish elevations, at times involving the solitary follicles or Peyer's patches, at times not. Superficial necrosis frequently occurs, leaving an ulcer with a fibrous base and very slightly elevated edges. The ulcers usually extend in a direction at right angles to the axis of the bowel, and at times lead to stenosis. Kundrat and Moerek have reported the perforation of a syphilitic ulcer.

In acquired syphilis, symptoms of enteritis at times occur early in the disease, which may be of the nature of intestinal manifestations comparable to the secondary cutaneous manifestations. Pathological observations of the condition are wanting. Later in the disease intestinal lesions are observed similar to those observed in congenital syphilis, excepting that they are more common in the large intestine than in the small. They appear first as grayish-red, smooth, gummatus elevations, which later undergo necrosis resulting in flat, sharply marginated ulcers, with a smooth, translucent, gray or yellow base. As in the congenital lesions, they tend to extend around the lumen of the bowel and cicatrize, thus producing stenosis. Occasionally perforation occurs.

The most frequent situation of syphilitic ulceration of the intestines

is in the rectum and particularly in its terminal portion just above the sphincter. The ulcers are distinguished from those of dysentery by their smooth, gray base and the tendency to induration of the edges and extensive stenosis. It is probable that stenosing tuberculous ulcers of the rectum have been frequently mistaken for syphilitic lesions. Syphilitic rectal stenoses are more common in women than in men. They may result from the cicatrization of a primary lesion, of mucous patches, or of ulcers caused by necrotic gummata.

The *symptoms* of syphilitic involvement of the intestines are those of simple intestinal ulceration or stricture and permit a probable diagnosis only on the basis of the history or the associated findings of syphilis, and possibly their response to the therapeutic test. Syphilitic stenoses of the rectum are distinguished by the marked induration and extensive cicatrization.

The *treatment* is directed to the general infection and to the control of the diarrhoea. The latter often persists in spite of ordinary treatment and until active antisyphilitic remedies are employed.

### AMYLOID DISEASE OF THE INTESTINES

This occurs as a result of the same causes that produce amyloidosis elsewhere. The most prominent causes are chronic tuberculosis, syphilis, chronic suppuration, and the various cachexias. In point of frequency, the intestines stand fourth among the organs affected, the kidneys, spleen, and liver being the organs more frequently involved. Usually the entire intestinal tract is diffusely affected, but at times the ileum only is the seat of the disease. More rarely the colon alone is affected. The process may involve any or all of the tissues composing the intestinal wall, but seldom affects the mucous membrane itself. The lymphoid follicles usually remain entirely free from the amyloid involvement. The diseased intestine presents a pale, shiny, translucent appearance, and gives the typical amyloid reaction.

A feature of amyloid disease of the intestines requiring special mention is the so-called *amyloid ulcer*. These are described as ulcers varying in size from that of a pinpoint to that of large areas involving the entire circumference of the intestines in a girdle-like fashion, and from 5 to 15 cm. in length. They have smooth, slightly thickened edges and a pale base with numerous small striations. It is possible that a simple ulceration occurs as a result of the insufficient nutrition of the surface epithelium caused by the amyloid degeneration of the underlying vessels. It is not improbable that some of the ulcers described as amyloid were tuberculous ulcerations occurring as one of the manifestations of the disease producing the amyloidosis.

Mild degrees of amyloid disease present no *symptoms* by which it can be recognized clinically. More severe grades present one constant feature—diarrhoea. The stools are moderately frequent and watery, but present no characteristic features. The cause of this watery diarrhoea has been variously attributed to anemia of the intestinal wall, to increased



permeability of the vessel walls, and to decreased absorptive powers of the intestinal mucosa. The question of the presence of blood in the stools in amyloidosis of the intestines is one of considerable importance. Colberg, claiming amyloid ulcers to be a common association of diffuse amyloid disease of the intestines, looks upon the presence of blood in the stools as a diagnostic feature. The probabilities are, however, that the presence of blood in the stools points to the existence of other conditions than simple amyloidosis. Pain and tenderness play no part in the symptomatology of uncomplicated amyloid disease of the intestines. The *treatment* resolves itself into that of the primary disease and an attempt to control the diarrhoea, which is best accomplished by the mineral and vegetable astringents and opium.

### SPRUE

Sprue, or psilosis, is a form of chronic inflammation of the gastro-intestinal tract met with in certain tropical countries—notably in the Orient—characterized by great weakness and wasting, anemia, and a chronic form of diarrhoea.

**Etiology.**—The essential nature of the disease has not yet been determined. According to Scheube, it never occurs epidemically and is not contagious. The disease occurs only in hot climates and affects Europeans who have resided for some time in such climates more frequently than natives. The disease may occur without any predisposing cause, but often follows exhausting conditions.

**Pathology.**—The lesions consist in a catarrhal inflammation, followed by erosions and atrophic changes affecting the whole gastro-intestinal tract. The mucous membrane of the mouth may present an inflamed surface, with erosions and aphthous spots. The small intestine is usually extensively involved, and the colon may present distinct ulcerations. When it has continued for some time, secondary changes may be met with, such as marked atrophy of the mucous membranes, areas of distinct erosion, and sometimes small, cystic dilatations of the intestinal glands. Enlargement of the mesenteric lymph nodes is frequent.

**Symptoms.**—The onset may be gradual or abrupt. In many cases it occurs in the course of other diarrhoeal diseases. The patient presents a wasted, anemic appearance, and the evidences of severe secondary anemia are found. Abdominal distension occurs and may cause a reduction in the extent of liver dulness.

The most characteristic features are those affecting the gastro-intestinal tract. The tongue and mouth become sore from exfoliation of the mucous membrane and the formation of herpetic or aphthous lesions. The term "Ceylon sore mouth" has been applied to this condition. Dyspeptic symptoms and flatulent distension of the stomach are frequent. The characteristic diarrhoea soon develops, and continues, with exacerbations and periods of quiescence, throughout the disease. The stools are large, usually loose, of a light grayish or white color, and frequently frothy. Chemical examinations show an increase of mucus and some albumin,

as well as an excessive quantity of fat. Quantitative analyses indicate that intestinal absorption is much diminished. The clinical course is a chronic and remitting one, periods of active intestinal symptoms alternating with intermissions of quiescence.

**Prognosis.**—Cases recognized and treated early usually recover, although the tendency to relapse is very pronounced. Fatal cases terminate as the result of continued diarrhœa, lack of digestion and absorption of food, and consequent inanition.

**Treatment.**—Strict regulation of the diet offers the best chance of recovery, particularly if instituted early. A strict milk diet kept up for several weeks appears to be most generally advisable. Cantlie has recommended a pure meat diet, and sometimes the administration of fresh fruit or berries. Drugs, excepting such as are used for symptomatic treatment, have little value.

## INTESTINAL OBSTRUCTION

**Definition.**—The term intestinal obstruction is here used to signify incomplete or complete interference with the onward movement of the intestinal contents and their eventual discharge, occasioned by some form of mechanical or structural impediment of more or less limited extent. The term does not apply to interference with the passage of the intestinal contents caused by the general weakness or paralysis of the bowels or by the conditions of the contents themselves, which are referred to in the discussion on *Constipation* and *Intestinal Obstruction due to Motor Paralysis of the Bowel*. A variety of terms have been introduced to designate different kinds of obstruction:

*Ileus* is an ancient name, variously applied to paralytic conditions of the intestines, to obstruction in a general sense, or to obstruction with feculent vomiting. It is rarely used at the present day, and on account of its indefiniteness should be abandoned.

*Occlusion* implies a complete closure of the intestinal lumen.

*Stricture* signifies a contraction of the lumen caused by disease of the wall, usually involving its entire circumference in a more or less limited section.

*Constriction* signifies a narrowing by adhesions, fibrous bands, or similar conditions outside the bowel.

*Obturation* signifies an obstruction of the lumen of the intestines by contents, foreign bodies, or other conditions inside the bowel.

*Compression* indicates obstruction due to the pressure of tumors, misplaced organs, or other conditions outside the bowel.

*Incarceration* indicates an obstruction, more or less complete, from the retention of a coil of intestine beneath fibrous bands within hernial sacs, etc.

*Strangulation* indicates the constriction of a coil of intestine in which more or less complete obstruction of the bloodvessels supplying this coil has taken place, causing intense venous stasis.

Intestinal obstruction may be acute or chronic. Frequently, after

partial chronic obstruction, there is an acute increase of the obstruction, and clinically, difficulty is experienced in distinguishing such cases from acute obstructions.

**General Pathology.**—Certain conditions affecting the bowel and its immediate connections, the peritoneum, the mesentery, etc., result from obstructions of all sorts without reference to the precise morbid condition that has occasioned the obstruction. Characteristic differences are met with in the anatomical conditions occurring in chronic cases, as contrasted with those of acute character.

**Chronic Obstruction.**—A striking contrast is seen in the condition of the bowel below and above the point of obstruction. Below the obstruction the intestinal coils are empty and contracted, and their color more or less grayish or white. The condition is that seen in the empty intestine of persons who have died of inanition. Sometimes remnants of the intestinal contents remain in the contracted bowel below the obstruction, especially when hardened fecal masses had been present at the time of the obstruction and, on account of their physical character, could not readily be transported onward. Above the obstruction the bowel is distended, and, after a certain length of time, elongation, thickening from hypertrophy of the walls, ulceration, and other inflammatory changes in the mucous membrane and serous coat may be met with.

The first effect is the accumulation of contents above the constricted area, and a resulting dilatation of the bowel. Later, this distension seeks higher and higher levels, until almost the entire intestinal tract above the constriction may be involved. The distended bowel contains fluid or somewhat consolidated fecal matter, according to the situation of the obstruction. In cases involving the small intestine, fluid contents alone are met with. In obstruction of the large intestine there may be semisolid or even solid fecal masses. This, however, is not invariable, as the contents may be fluid even in obstruction of the lower part of the large bowel. A certain amount of gas may be present, but distinct accumulations of gas are unusual, as the gases are absorbed from the mucous membrane so long as the circulation of the bowel has not been seriously disturbed. Moreover, gases are usually able to pass beyond the obstructed area after any onward movement of fluid or solid feces has become impossible.

Hypertrophy of the wall of the bowel follows and this affects the muscularis especially, and may be confined to this part, although some thickening of the other tunics may also occur. Experiments in animals have shown that the hypertrophy begins as early as the fourth or fifth day after obstruction of the bowel has been established, and is quite marked by the ninth day (Herczel). The hypertrophy is due to an increase in the width of the muscle fibres rather than to increase in their number. It is a functional hypertrophy which, to a certain extent, enables the bowel to overcome the obstruction.

Changes in the mucous membrane result from the stasis of the contents and secondary fermentative or putrefactive changes. As a result of the irritation, inflammatory conditions and finally ulceration of the mucous membrane and submucosa occur. Formerly the direct



mechanical irritation of retained contents, and especially of hardened masses, was considered of prime importance in the development of such ulcers, and the names stercoral ulcer and decubital ulcer were applied. According to Kocher, a better term would be distension ulcer, as he regards the ulceration as due to overdistension of the intestines with consequent disturbance of circulation. When inflammatory changes are pronounced the mucous membrane may be somewhat thickened, but nearly always it is thinner than normal. The serous coat is thinned by the distension, and more or less stretched in a longitudinal direction as the result of a shortening of the mesentery by the dilated bowel.

**Acute Obstruction.**—When this has followed a chronic but only partial occlusion, more marked distension of the bowel above the obstruction occurs as the result of suddenly increased pressure and interference with the movement of the contents, causing the accumulation of gases.

In purely acute cases there are quite marked differences from those met with in chronic obstruction. Below the obstructed area the bowel is empty and contracted, as in chronic cases. Above the obstruction the principal change is distension, with great thinning of the walls of the bowel. There is no evidence of hypertrophy, such as occurs in the chronic cases owing to the acuteness of the condition. The contents of the bowel are, in the beginning, liquid or semiliquid, but after a relatively short time gaseous accumulations occur as a result of interference with the circulation and consequent cessation of absorption from the mucous surface, and also as a result of the inability of the gases to pass the acutely obstructed portion. Paresis of the bowel is favored by interference with the circulation and a hyperemic condition of the walls of the gut. When complete stasis of the circulation has developed, absorption of accumulating gases ceases and increasing dilatation occurs. The gases are partly derived from the air swallowed with food and in part from fermentative processes. A considerable part of the distension may, however, be due to carbon dioxide derived from the venous blood.

The condition of the bowel in strangulated coils is of particular importance. The obstruction of the circulation in such portions produces a rapid hyperemia, and eventually a complete stasis of the circulation. The coil becomes of a deep red or purplish color and is tensely distended. Hemorrhagic extravasation may occur within the lumen or on the outside. A gangrenous condition may develop, when the intestine becomes of a greenish or grayish color. Occasionally obstruction of the arteries as well as of the veins may cause a somewhat different appearance, the bowel in these cases remaining flaccid and becoming gangrenous in a very short time. The strangulated coil undergoes rapid distension from the accumulation of gases.

Affections of the peritoneum may occur in cases of strangulation or in other forms of intestinal obstruction due to the escape of micro-organisms through the wall of the bowel in the area of obstruction, or immediately adjacent to it. The local conditions (compression of the tissues by bands, intussusception, etc.) and the complete stasis of the circulation cause degenerative changes in the wall of the bowel and make them more readily permeable, and thus a rapid involvement of

the peritoneum becomes possible. In cases of gangrene and perforation of the intestines a violent local or perhaps general peritonitis quickly supervenes, and foul-smelling collections of inflammatory exudates and necrotic material with escaped intestinal contents are encountered.

**General Symptomatology.**—The important clinical manifestations of obstruction of the intestines are pain, distension, nausea and vomiting, constipation, prostration, and collapse. A variety of secondary symptoms or variations in the manifestations occurs in the different types.

**Pain.**—This differs greatly in manner of onset, severity, and character, according to the acuteness of the case. In acute obstruction sudden abdominal pain, usually of considerable violence, is the rule. This may be occasioned by the direct irritation of the nerves in the affected segment, by the sudden compression or obstructive cause, and by the violent peristaltic efforts above the obstruction. As acute obstruction more commonly involves the small intestine than the large, the pain is more likely to be general than localized, as it is well known that the nervous mechanism prevents an accurate localization of pain involving the small bowel. In the majority of cases the pain of onset is referred to the middle portions of the abdomen. At first it is intense and may continue so until, as a result of exhaustion, or possibly of toxemia caused by the absorption of putrefactive products, a cessation is brought about. The pain may be so severe in the beginning that nausea, vomiting, or profound prostration may result. After an interval of cessation, secondary pains of cramp-like or colicky character due to violent peristalsis set in. These, however, are rarely prolonged, as are the pains met with in chronic obstructions. Very soon the bowel becomes fatigued, or prostration reaches a grade that puts an end to the patient's suffering.

Extension of infection to the surrounding peritoneum may add a new form of pain, sometimes distinguishable by its stabbing character and by its association with local tenderness and other symptoms. In other cases rapid abdominal distension may be the occasion of general abdominal pain described as of a rending character.

In *chronic* obstruction, pain may be wanting for a long time, and nearly always its onset is somewhat gradual. The patient first becomes aware of slight abdominal discomfort due, apparently, to some interference with the movement of the contents of the bowel, and especially gases. Later, these sensations increase to a more definitely painful form; or, when there is a sudden increase in the degree of obstruction, intense, cramp-like paroxysms may set in. Not rarely the earlier symptoms have been so indefinite and uncertain that the occurrence of an entirely acute obstruction is suggested. The attacks of pain may become so severe that the patient screams or doubles up in agony. He is conscious of a more or less fixed location, and may feel the cramps begin at one portion and move more or less quickly to the place of obstruction, where the bowel becomes tensely distended, sometimes forming a visible hard mass. This indurated segment of the bowel may be so hard that on palpation it seems almost like a solid tumor. After a variable duration it relaxes, and relief may be obtained for a greater or less period of time. After a certain duration the colicky pains of chronic obstruction may

subside and there may be an interval of hours, days, or even weeks before another attack sets in.

Associated with the paroxysmal pains of chronic obstruction is a symptom of extreme importance, namely, visible peristalsis. This may be seen through thin abdominal walls in persons not suffering with intestinal obstruction, but these movements are slow vermicular contractions, visible over a greater or less extent of the abdominal surface. They differ very decidedly from the intense and usually rapid waves met with in obstruction, and on palpation there is never the stiffening and evident tonic contraction found in cases of occlusion.

Meteorism is usually somewhat late in development, except in acute cases with strangulation and rapid interference with the circulation of more or less extensive segments of the bowel. In chronic cases there may be but little distension until near the termination of the case, when complete obstruction has developed and paresis of the bowel above the obstructed area has caused interference with the circulation. Up to the very end the amount of distension may be relatively small. In acute cases, with marked interference of the circulation, rapid and intense meteorism may cause early abdominal distension. In conditions of strangulation of coils of the intestine, paralytic distension of the strangulated area may occasion local meteorism of marked grade.

**Constipation.**—All forms of intestinal obstruction interfere with the onward movement of the intestinal contents. The resulting conditions vary considerably in different cases. In *acute* obstruction a sudden cessation of all intestinal movements may occasion an immediate absolute constipation, although frequently a movement or two may empty the lower bowel before the constipation becomes absolute. The higher in the intestinal tract the seat of obstruction, the more likely are some movements of the bowel to occur, after the development of the condition. The reasons for this are that the contents in the bowel below the point of obstruction may be discharged after the obstruction has taken place, and also that the fluid contents of the upper intestine are more likely to pass a partial obstruction than are the semisolid or solid masses of the lower bowel to escape through an obstruction in that region. In partial obstructions in the small intestine continuous diarrhoea with passage of peculiarly offensive stools is not unusual.

In *chronic* obstruction, especially that involving the large intestine, constipation is sometimes absent or insignificant. In these cases the gradual development of the obstruction and the compensating hypertrophy of the musculature above the occlusion make it possible for the contents to escape in an approximately normal manner. Sometimes considerable accumulations of fecal matter may be found above an area of obstruction in cases in which the movements of the bowels have seemed approximately or wholly normal. Much importance has been thought to attach to the character of the stools in cases of partial obstruction of the lower bowel. Among other forms, small, separated, spherical masses and ribbon-shaped formations, or narrow, pencil-like stools, have been particularly noted. It is undoubtedly true that partial intestinal occlusions do occasion formations of this character; but exactly



the same conditions may occur without any organic obstruction whatever, especially in cases of constipation due to local spasm of the bowel in cases of spastic contraction of the sphincter, etc. The presence of blood, pus, and mucus with the bowel movements is not infrequent in obstructions due to organic conditions involving the lower bowel, especially in carcinoma and intussusception.

**Diarrhœa.**—This may occur in intestinal obstruction, instead of constipation, and easily occasion a mistake in diagnosis. This is particularly liable to occur in chronic cases and is occasioned by the occurrence of inflammatory conditions of the mucous membrane above the obstruction. Some have believed that diarrhœa is always significant of ulceration, a view that is certainly not invariably correct. The diarrhœa may be continuous and chronic, or may be recurrent. The character of the movements varies, but there is usually a tendency to a considerable admixture of mucus. When ulceration exists, blood and pus may also occur in the movements.

**Vomiting.**—Soon after the development of intestinal obstruction, whether complete or only partial, nausea and disturbance of the stomach occur, and in many cases vomiting sets in quite promptly. In cases in which there has been marked pain, the nausea and vomiting are in a measure dependent upon the intensity of the suffering, and are clearly reflex. The character of the vomiting varies at different stages. At first the contents of the stomach are brought up, and sometimes, when the stomach has been overloaded at the moment of an acute obstruction, considerable relief follows the primary vomiting. Usually, however, vomiting continues without cessation, and after the food contained in the stomach has been discharged, watery fluid or bile is brought up. Eventually stercoraceous or fecal vomiting takes place, and is the most characteristic symptom. In the beginning the fecal odor is merely suggested. Soon, however, it becomes unmistakable. Finally, quantities of liquid vomit, of the foulest character, are discharged, sometimes with violence, while in other cases it gushes from the mouth.

A great deal of discussion has taken place regarding the causes of the fecal vomiting. Formerly various theories were entertained, such as those which attributed it to reversal of the peristalsis and to transportation of intestinal contents to the stomach from portions of the intestine just above the obstruction. There is no doubt that such antiperistalsis may occur, and that accumulated matter in the lower part of the small intestine may be brought to the stomach and vomited. Brinton suggested that, while the ordinary peristalsis carries the contents adjacent to the walls of the bowel forward in the usual manner, a reversed axial current is taking place at the same time. Investigations regarding the whole subject, and a consideration of the functions of the different portions of the intestinal tract, suggest that the symptom is due to the accumulation of secretions in the small intestine, and eventually an overflow. Obstruction in the large intestine, especially when low down, may be unattended with this symptom from first to last, or accompanied by it only late in the course, because absorption still goes on in the portion of the large bowel above the obstruction.

Occasionally stercoraceous vomiting may occur in gastro-intestinal diseases, unattended with intestinal obstruction, functional or organic. In these cases bacterial decomposition of gastric contents, and especially of blood mixed with other gastric contents, may cause the suggestive odor. The organism most likely to produce this is the *Bacillus coli*.

In cases of obstruction situated near the upper end of the small intestine, the vomiting may be characterized by the intense violence of the straining efforts, by the comparatively small amount of matter brought up, and by the tendency to speedy collapse. In cases of obstruction of the large intestine, and in chronic obstruction generally, vomiting is much less pronounced than in acute cases and those in which the small intestine especially is involved. Sometimes there may even be little nausea until a late stage has been reached, and the vomiting is usually rather closely dependent upon the taking of food, attempts at sitting up, or other movements or efforts. In the late stages, when violent attacks of colic have developed, vomiting of the same character as occurs in acute obstruction develops.

**Prostration and Collapse.**—In acute cases collapse may set in very promptly. In chronic forms of obstruction it may be absent until the final stages have been reached. The most intense and sudden collapse occurs in cases in which the obstruction is situated high up in the small intestine. It is due to the sudden injury sustained by the nerves of the bowel, and is proportionate to the pain, retching, and other symptoms caused by the same nerve injury. It is, therefore, in the nature of a shock to the abdominal nervous system. There may be equally sudden prostration and collapse in obstructions situated lower in the small intestine; but more usually in these cases the patient becomes gradually weaker until finally he passes into a state of collapse. In chronic obstruction collapse may be late, and does not usually present itself until decomposition of retained products and toxemia have occurred.

The appearance of the patient suffering with prostration and approaching collapse from intestinal obstruction is often characteristic. The skin is cold, pale, and generally bathed in sweat. The face wears an expression of anxiety and is pinched. The temples appear sunken. The eyes are depressed in their sockets and surrounded with dark rings. The respirations are shallow and often sighing. The temperature of the body falls. The pulse becomes rapid, feeble, and finally thready and irregular. The mucous membrane becomes dry, so that the mouth is literally parched. Urinary excretion diminishes until it may become suppressed. Finally, the patient sinks into a state of torpor, or complete stupor or coma. Before this stage is reached the increasing toxemia and infection cause a cessation of all sensation, and the acute sufferings of the earlier stages subside. Sometimes the obtunding of sensory acuity develops without other manifest evidences of collapse, and may occasion a deceptive appearance of improvement.

The causes of collapse in intestinal obstruction are: (1) the primary shock to the nervous mechanism of the intestine; (2) repeated vomiting and loss of water from the system; (3) intoxication and infection. The

loss of water through vomiting and sweating may operate directly by reducing the strength of the patient, and indirectly by inspissation of the blood. According to Nothnagel, the concentration may reach 24 per cent. of the total volume of blood.

The toxemia of the late stages is doubtless caused by a large variety of substances generated by the decomposition of retained materials in the intestinal tract. As this takes place with greatest activity in the large bowel, toxic prostration and collapse are more marked in the cases in which the obstruction is situated in some part of the large bowel. Repeated vomiting and consequent inanition may lead to acid intoxication by the destructive decomposition of the fats of the body and the manufacture of acetone bodies or in other ways. Direct bacterial infection adds to the prostration of the patient and coöperates with the toxic causes of collapse.

**Diagnosis.—General Diagnosis.**—The existence of intestinal obstruction is usually rather easily determined, when the symptoms that have been mentioned present themselves. In acute cases the sudden occurrence of pain and the development of nausea and characteristic vomiting, the obstinate constipation, and the final prostration or collapse leave little doubt. There are cases, however, in which, although the development of obstruction has been acute, some of these symptoms are poorly developed. On the other hand, there are conditions in which very similar symptoms are occasioned by diseases outside the intestine itself, although doubtless affecting the bowel in an indirect or reflex manner.

**Differential Diagnosis between Intestinal Obstruction and Conditions Simulating It.**—1. Various conditions may occasion sudden intense pain, with nausea, vomiting, and collapse. Among such conditions are the passage of biliary or renal calculi, the rupture of gastric and duodenal ulcers, torsion of the pedicle of a movable spleen, crises in cases of movable kidney, pancreatic hemorrhage and acute pancreatitis, embolism or thrombosis of the mesenteric vessels, and nervous crises associated with locomotor ataxia or other nervous diseases. In all these cases the symptoms of onset may be similar to those met with in cases of intestinal obstruction. If, as a result of the violent irritation of the nervous system, a reflex paralysis of the intestine occurs, an actual intestinal obstruction may develop. Usually, however, in the conditions named, although there is some weakening of motility of the bowels and consequently a certain degree of constipation, the obstruction is not absolute, and enemata rarely fail to bring away a certain amount of fecal matter. Distension of the abdomen, if it occurs, is only of moderate grade. The vomiting, although perhaps urgent in the beginning, does not persist as in obstruction, and rarely is fecal.

2. In a second group intestinal obstruction is suggested by the occurrence of absolute constipation. In a certain sense these cases are truly instances of actual obstruction, although the conditions differ from those of intestinal obstruction in the ordinary sense. In this group may be included the paralytic condition of the bowel following pronounced forms of peritonitis. The onset of such cases, the early development of fever, the leukocytosis, and other evidences of infectious inflammation



are important. The vomiting rarely becomes fecal and constipation is not, as a rule, absolute.

In chronic and tuberculous peritonitis, intestinal distension, constipation, and vomiting may suggest obstructed conditions of the bowel. The clinical course, however, is more prolonged; there is less vomiting than in obstruction, rarely ever fecal vomiting; and the degree of constipation is rarely as great as in obstruction. Direct examination of the abdomen will usually detect local indurations, fluid exudate, or enlarged mesenteric glands.

3. In a third group of cases intestinal obstruction is suggested by the marked degree of abdominal distension, associated with some other, although less conspicuous, symptoms suggesting obstruction. Thus in cases of infectious disease, such as typhoid fever, pneumonia, and violent acute intoxications, and infections of the bowel itself (enterocolitis), progressively increasing abdominal distension, together with nausea, vomiting, and constipation may cause a close simulation of certain forms of obstruction. In these cases, however, vomiting never becomes fecal in type, the degree of prostration and collapse is less pronounced, and the constipation is rarely absolute, so that the use of enemata usually suffices to obtain some fecal discharge.

In the case of certain nervous conditions, notably hysteria, marked distension of the abdomen (phantom tumor) may occasionally occur. In these cases there is often a striking lack of other symptoms, and the distension not rarely varies very quickly. Under psychic influences, and when the patient is asleep or is anesthetized, such abdominal distensions may suddenly subside. Similar distension of the abdomen may occur in patients suffering with locomotor ataxia; but in these cases severe abdominal pain and sometimes associated gastric crises attended with vomiting are more apt to be present.

**Diagnosis of the Situation of the Obstruction.**—Obstruction in the uppermost portion of the duodenum may present the features of pyloric obstruction. When the occlusion is below the outlet of the bile-duct intense vomiting with constant presence of bile is a striking feature. The vomit does not in this case become stercoraceous. When the point of obstruction is in the jejunum or ileum the gastric symptoms though often marked do not so wholly dominate the symptomatology. The pain is less definitely localized, the vomiting becomes stercoraceous earlier, and suppression of urine is a more marked and earlier manifestation than when the obstruction is situated in the large bowel. Stiffening of segments of the bowel in the central portion of the abdomen and the narrowness of the palpated coils may indicate that the obstruction affects the small intestine. Obstruction in the large bowel usually occasions a more reliable localization of pain and tenderness, and the passage of mucous movements or blood and mucus are significant. When tonic peristaltic contractions of the bowel, with violent attacks of colic, set in, these may sometimes serve to locate the place of obstruction, as the wave of contraction may move indefinitely through the abdomen until it reaches the point of obstruction, where it produces a stiffening from tonic spasm, and sometimes a hard tumor-like mass.

This point may be recognized by the patient himself and accurately located by him; or it may be seen through the abdominal walls or felt in palpating the abdomen. Obstructions in the lower part of the large intestine, especially in the rectum, may occasion ribbon-shaped or pencil-like stools for some time before the obstruction is complete.

**Fluoroscopic and Skiagraphic Methods of Diagnosis.**—The diagnosis of the site and sometimes the kind of obstruction has been greatly facilitated by these methods, which are particularly available in cases of partial and chronic obstruction. In cases of obstruction in the small intestine or in the upper part of the large intestine examinations at various time intervals after administration of bismuth meals give the best results. When the obstruction is low down in the large intestine bismuth enemata may prove more satisfactory. In the study of the plates care must always be exercised to determine whether the point of obstruction is indicated in several plates so as to avoid confusing a temporary stagnation for a fixed condition. Fluoroscopic examinations are particularly valuable in enabling the examiner to determine adhesions between neighboring coils of intestine or between the bowel and other structures. They are also helpful in showing delayed emptying of the stomach in cases of duodenal stricture or obstructions to the entrance of the bismuth enema in cases of obstruction in the lower bowel.

**Urine.**—The time of occurrence and the degree of indicanuria have been utilized as indications of the seat of obstruction. The early appearance of indican is undoubtedly of value in locating the obstructed point in the small intestines provided that other causes of indicanuria can be excluded. The amount of urine has been referred to as sometimes significant. The higher the obstruction is situated in the small intestine the more intense will be the vomiting, and, consequently, the greater the loss of water from the system. At the same time, there is a failure of the absorption of liquid from the lower bowel. Therefore, an early reduction in the quantity of urine is significant of obstruction high up in the small intestine.

**Obstruction Due to Foreign Bodies or Fecal Masses.**—Among the causes included under this heading are gall-stones, intestinal calculi and parasites, various foreign bodies, and masses of fecal matter.

**Gall-stones.**—These are a rare cause of intestinal obstruction, as their size is only infrequently sufficient to obstruct any portion of the intestinal tract. They may, aside from direct obstruction, be the occasion of volvulus or of obstruction resulting from adhesions between the gall-bladder and some portion of the intestinal tract. The proportion of cases found by various authors ranges from 1 in 15 (Fitz) to 1 in 28 (Leichtenstern). The gall-stone usually finds its way into the intestine through a fistulous connection between the gall-bladder and the intestinal tract. Less commonly, it slowly works its way along the common duct, ulceration opening the way before, and cicatrization contracting the channel behind the calculus. After reaching the intestine, the stone may cause obstruction of the duodenum, or it may move downward into the jejunum or ileum and become impacted there. The most common situation of impingement is in the lower part of the ileum, near

the ileocecal valve. In some cases the stone caused obstruction of the large intestine.

**Symptoms.**—The clinical manifestations may be divided into two stages: the first, in which active symptoms result from the escape of the calculus from the gall-bladder or the biliary passages into the bowel; and the second, in which intestinal obstruction occurs. In the first stage, violent attacks of colicky pain attended with jaundice are characteristic. These symptoms may have been preceded by a clinical history suggestive of the presence of biliary calculi. After entering the bowel, evidences of partial and temporary, followed by complete, occlusion may present themselves. As the stone usually finds its way first into the upper part of the small intestine, the symptoms, such as vomiting and colicky pain, are comparatively severe. After a little while these may be relieved, but they may be renewed with each successive lodgement in positions lower down, until finally a complete impaction occurs in the ileum, and the evidences of total obstruction make their appearance. Even after complete impaction the calculus may be dislodged, the symptoms relieved, and the stone discharged from the bowel. In cases in which relief does not occur, death usually takes place between the fifth and the tenth day, but sometimes later. The outlook is always grave, as approximately half of the patients succumb.

**Intestinal Concretions.**—Intestinal concretions of sufficient size to produce obstruction are exceedingly infrequent. They consist of organic substances such as mucus, masses of bacteria, and fatty constituents impregnated with calcium and magnesium salts. Such concretions are usually formed in cases of enteritis, and the symptoms are therefore preceded by those of this condition. Gradually, as the foreign body enlarges, the attacks of colic, diarrhoea, and other evidences of enteritis become altered and give place to the evidences of more or less complete occlusion. In case of the formation of concretions in pouches of the bowel, especially of the large intestine, evidence of partial obstruction are met with, and a continuous intestinal irritation or colitis is encountered.

**Foreign Bodies.**—Foreign bodies other than those described are comparatively rare causes of occlusion. Fruit-stones, masses of intestinal parasites, hardened accumulations of mucus, balls of hair or vegetable fibre, and accumulations of medicinal substances, such as bismuth, salol, chalk and other insoluble substances taken by the mouth, may occur. Such obstructions are at first partial, and may continue so for a long time. Hardened masses located in the lower part of the large intestine may set up catarrhal irritation and occasion a diarrhoea which confuses the diagnosis. More commonly, fecal matter accumulates above and around the foreign body until more or less total obstruction has resulted.

**Obstruction Due to Bands.**—Intestinal obstruction may result from the constriction of a portion of the bowel by a band or adhesion formed by a previous inflammatory condition, or by various abnormal bands of fibrous tissue that result from developmental conditions. In a similar manner a Meckel diverticulum may be the occasion of this form of occlusion. Subsequently a coil of intestine may become constricted by



passing beneath or over such a band, and the distension of the portion of the coil beyond the band may prevent its escape.

A Meckel diverticulum is quite a frequent cause of obstruction, having been met with in 21 of the 669 cases at the London Hospital. If the diverticulum remains connected with the umbilicus, the conditions are such that obstruction of a coil of intestine may readily be produced; still more, when the free end of a diverticulum has formed a new attachment to the mesentery or some other part in the abdomen. A coil of bowel passing over or beneath the diverticulum may become twisted upon itself (volvulus), or may become variously knotted or contorted. Besides Meckel's diverticulum, bands may be formed by the attachment of the tip of the appendix to the appendices epiploicæ, the Fallopian tubes, or other structures within the abdomen, and strangulation of a loop of intestine may be the result. Occlusion by internal bands usually involves some part of the small intestine. The large bowel is relatively fixed and the lumen is such that strangulation beneath a band is infrequent. A coil of bowel may be held beneath a band for some time without symptoms. When, however, fecal accumulation or gaseous distension has increased its size, obstruction may occur and may rapidly increase from pressure upon the veins and consequent stasis.

**Symptoms.**—These are usually sudden and acute, and frequently follow after some strain or effort, or after acute digestive disorders with distension of the intestinal tube. The symptoms are those of acute obstruction from any cause, beginning with sudden pain and marked nausea and disturbance of the stomach. The evidences of obstruction follow rapidly, and the patient suffers early prostration and collapse. In many cases, however, the onset is less acute, and the symptoms are less violent. In these instances, pain and gastric disturbance may develop gradually and distension increases progressively. Evidence of more or less obstruction may be found, but the nature of the obstruction may be quite uncertain. When a coil of intestine is strangulated by a band, the occluded portion tends to undergo pronounced distension from the accumulation of gases and the retention of its contents; and a painful swelling may be felt through the abdominal walls. The distension may be so great that this is quite hard, and the percussion note over it may be relatively dull, from the tenseness of the walls.

**Obstruction Due to Internal Hernia.**—The term internal hernia is applied to hernial displacements of the intestines into the subperitoneal or retroperitoneal spaces without any protrusion externally. Among the *situations* in which they may occur are: (a) The subperitoneal tissue in the region of the inguinal rings, when the hernia may be associated with external hernia or independent of the latter. Not rarely such hernias have resulted from the reduction *en masse* of an external hernia. (b) Duodenojejunal hernia, a protrusion of part of the jejunum into the retroperitoneal tissues on the left side of the abdomen, beneath the crescentic fold of peritoneum, the plica duodenojejunalis. A number of such instances have been reported, and occasionally strangulation has occurred. (c) Pericecal herniæ, in which group are included hernias into the various pericecal or retrocecal pouches. (d) Intersigmoidal

hernia, a form of considerable rarity, in which the hernial sac occupies the fossa occasioned by the sigmoid artery. (e) Herniæ of the foramen of Winslow, in which portions of the small intestines or, more rarely, of the large bowel extend through Winslow's foramen. (f) Herniæ into Douglas' pouch. (g) Herniæ projecting into the broad ligament of the uterus. (h) Diaphragmatic herniæ.

The last-named is the most frequent and most important form of internal hernia. Leichtenstern compiled 252 cases, and Grosser published anatomical descriptions based upon 433 cases reported in the literature up to 1899. Struppler found the number of cases reported up to 1901 to be 500. A distinction is made between true and false diaphragmatic hernias, the former being cases in which the abdominal viscera extend through an opening in the diaphragm covered by a sac composed of peritoneum, pleura, or both. The false variety is that in which a free connection exists between the thoracic and the abdominal cavity (eventration). The latter variety is the more common. Diaphragmatic herniæ may be classified, also, as congenital or acquired, the latter being more frequent, and usually the result of traumatism causing rupture of the diaphragm. They are usually found on the left side, and among the positions most commonly involved are the opening for the œsophagus and an area immediately behind the stomach. The stomach is most frequently displaced through the abnormal opening, next to which in point of frequency the colon, the omentum, or other parts of the intestinal tract may be involved. In exceptional cases the spleen, pancreas, or kidney is displaced into the thoracic cavity.

**Symptoms.**—Sometimes these are wholly wanting and a diagnosis may be made by the signs indicating the presence in the pleural cavity of air-containing viscera, and the restriction of respiratory movements on that side. Displacement of the heart may be more or less conspicuous. The condition resembles most closely a pneumothorax, which, however, is usually distinguished by the fact that it commonly involves the whole pleural cavity, and is frequently right-sided. The auscultatory phenomena, especially the occurrence of amphoric breathing when a fistulous communication with the pleural sac exists, are quite distinctive. Difficulty in swallowing, vomiting, and other gastric symptoms, and sometimes intestinal obstruction, may occur in diaphragmatic herniæ, and are not met with in pneumothorax. Transillumination of the stomach and skiagrams may be helpful.

**Obstruction by Incarceration of the Bowel in Slits or Holes.**—An occasional cause of intestinal obstruction is the passage of a loop of the bowel through a hole or slit in the mesentery or omentum. The mesentery is the most frequent site of such imperfections and Treves has described a spot between the ileocolic and terminal mesenteric artery which is normally thin and readily becomes patulous. A gradual perforation of such a weak space may occur, but more commonly the perforation results from some violent injury that forces a portion of the bowel through the weakened area. Occasionally congenital holes are encountered. Sometimes, after inflammatory conditions, adhesions

of the omentum and other structures may be so arranged that spaces are left between the adherent portions, and the bowel may be involved in these. The symptoms of obstruction due to this cause are similar to those of incarceration by bands of adhesions. They develop with great acuteness, and usually are violent in their manifestations.

**Obstruction Due to Peritoneal Adhesions.**—In this group are included cases in which the bowel is narrowed by peritoneal adhesions resulting from chronic peritonitis without strangulation of the circulation. The adhesions that produce such constriction may result from any form of peritonitis, such as that attending disease of the appendix, the pelvic organs, the mesenteric or other abdominal glands, or that associated with tuberculosis, cancer, etc. Similar adhesions may follow after operations, particularly when drainage has been required.

**Pathology.**—The constriction may be annular, causing a limited contraction of the bowel similar to that due to stricture of the bowel, or a kinking or irregular contraction may be produced by looping over the bowel. In some cases the obstruction is due to a matting together of neighboring coils of intestine, or to close attachments to the parietal peritoneum by adhesions or by contraction of the mesentery. Annular adhesion or cicatricial formation in the peritoneum may result from ulceration within the bowel, or may follow peritonitis.

Kinking of the bowel without any distinct annular stenosis may occur under a variety of conditions, in which, following a localized peritonitis, short and firm adhesions have formed between the bowel wall and the abdominal parietes or one of the abdominal viscera. In many instances such kinks are multiple. In some cases, although adhesions occasion no sharp angulation, they may interfere sufficiently with peristalsis to result in partial obstruction.

**Symptoms.**—There may be no symptoms despite very extensive adhesions or deformations, and sometimes, even in cases in which almost universal agglutination is met with, very little interference with peristalsis is encountered. When obstruction occurs, the symptoms are those of gradually developing intestinal stenosis. As in other forms of organic obstruction, the symptoms may come on in a gradual manner, or may develop rather suddenly with attacks of pain, violent and visible peristalsis, and distension. Tumefaction may be found at the seat of obstruction, owing to the distension of coils of intestine adjacent to or included within the zone of adhesion.

**Obstruction Due to Stricture of the Intestine.**—By this term is meant a narrowing of the bowel by changes in its wall. This definition would include all forms of new growths involving the bowel, as well as other disease processes affecting it. As here employed, it will be limited to cicatricial strictures which in the great majority of cases follow ulceration. Tumors and some other conditions causing narrowing of the lumen of the bowel (diverticula) will be discussed elsewhere. Of the various forms of intestinal ulceration those due to tuberculosis, stercoral accumulations, ulcer of the duodenum, dysentery, and syphilis are the ones that are prone to be followed by cicatricial strictures. Not rarely the strictures following tuberculosis are multiple. The hyperplastic form



has been considered in a separate place. In this there may be marked encroachment upon the lumen of the bowel, just as in carcinoma or other tumors. In cicatricial ulceration of tuberculous nature, annular contractions occur without great thickening of the coats of the bowel. Stricture following *duodenal ulcer* have the same general characters as the constrictions of the stomach or its pylorus resulting from gastric ulceration. Jejunal ulcers may have the same termination.

Strictures following stercoral ulceration are met with in various parts of the large bowel, especially at the flexures, in the cecum, and in the rectum. An annular scar, with more or less thickening of the wall of the bowel, is usually found in such cases. It is not improbable that secondary carcinomatous change occasionally originates in such lesions. Strictures following syphilitic ulceration are most common in the rectum. Marked thickening, with irregular scar formation and constriction, characterize these cases. Strictures following *dysentery* were formerly regarded as very common. Woodward found not a single case of stricture in the 9431 fatal cases of dysentery occurring among the Union troops. A few instances have, however, been reported in the literature. Strictures following various traumatic injuries of the bowel, or after sloughing due to intussusception, hernia, etc., are occasionally met with.

**Symptoms.**—When a stricture occupies the small intestine, the symptoms may be relatively inconspicuous, owing to the fact that the intestinal contents in this portion of the bowel are normally fluid, and, therefore, unlikely to become stagnated. The occurrence of diarrhœa in some of these cases has been referred to in discussing the general symptomatology. A stricture in the large bowel much more readily produces obstruction by the gradual accumulation of hard fecal matter.

**Diagnosis.**—This offers greatest difficulty in cases of stricture of the large bowel, with hyperplasia of the intestinal walls. In such circumstances a differentiation from carcinoma may be very difficult.

**Treatment.**—This is purely surgical, unless the stricture is of small calibre or situated high up, when careful attention to the condition of the bowel may prevent difficulty.

**Congenital Stenosis of the Intestine.**—This is not uncommon and the great majority of cases occur at the ano-rectal junction. Leichtenstern found the proportion of cases as follows: 375 at the ano-rectal junction, 75 in the small intestine, and 10 in the colon.

**Compression of the Bowel.**—Intestinal obstruction is sometimes caused by the pressure on relatively fixed portions of the bowel by tumors, displaced organs, etc. Frequently localized peritonitis, with the formation of adhesions, contributes largely to the obstruction. The rectum is the portion of the intestine most frequently compressed, 60 per cent. of Leichtenstern's cases having this location. Among the causes, fibroid tumors, carcinoma, and misplacements of the uterus are the most frequent, but abscesses, extra-uterine pregnancy, and other causes are also met with. Compression may also occur in other parts of the large intestine, or even in the small bowel. The *symptoms* are sometimes acute but in the majority of cases some evidence of chronic obstruction precedes the acute symptoms.

**Intussusception.**—Intussusception, or invagination, is a condition in which one portion of the bowel extends into a neighboring portion in such a manner that the former is ensheathed by the latter. The part of the bowel within the ensheathing portion is known as the *intussusceptum*, the outer portion as the *intussusciens*. On transverse section there will be found three thicknesses of bowel: (1) the outer, or ensheathing; (2) the returning part of the intussusceptum; and (3) the entering part. The term *neck* is applied to that portion of the intussusception where the intussusceptum passes within the ensheathing bowel. The doubling of the bowel where the intussusciens joins the returning layer of the intussusceptum is known as the *collar*. Occasionally an intussusception is incomplete, lateral, or partial when only a part of the circumference of the bowel is drawn into another part. Usually the intussusceptum extends downward into an intussusciens, but ascending or retrograde intussusceptions sometimes occur. The term compound intussusception has been applied to cases in which a second intussusception extends into the first, so that a section would show five or more layers of bowel.

**Etiology.**—A distinction should be drawn between agonal intussusceptions and the pathological variety. In the former, which are multiple, violent peristaltic contractions doubtless play an important part. In pathological intussusception independent of the agonal period, the explanation is usually to be found in some organic defect which occasions a prolapse of a segment of the bowel into a portion beyond; or in some pathological lesion of a part of the bowel which is carried downward into a portion beyond. Thus if a direct prolapsus of a portion of the bowel into a segment beyond occurs, the prolapsed portion is seized by the peristaltic contractions of the part into which it extends, and is carried forward in the same manner as intestinal contents are usually transported. In the same way a polypoid or other tumor of the bowel, an inverted Meckel diverticulum or appendix, or some other pathological condition, may occasion the beginning of an intussusception. A prolapsus of the ileocecal valve is a common cause.

Various investigations of the etiology of intussusception in cases in which no antecedent pathological lesion of the bowel has been found have indicated that the primary condition is a spasm of the circular muscle of the bowel in some portion. This constricted area is grasped by the segment immediately below, and thus starts the process that terminates in a complete invagination. A number of different developmental defects may predispose strongly to this condition, and may be the initial cause, as when there is an undue size of the large intestine as compared with the small and a consequent tendency to prolapsus. Abnormalities of the mesentery similarly predispose by permitting of the more ready invagination of one part of the bowel into another.

**Immediate Causes.**—The study of large series of cases of intussusception shows an absence of any definite immediate cause in half or even a larger proportion of the cases. In a relatively small number, some history of acute intestinal disturbance or of injuries is met with.

**Age.**—Intussusception is the most common form of intestinal obstruction in childhood and infancy. Among Leichtenstern's 593 cases, 131

occurred during the first year of life. In Weiss' 321 cases, 177 occurred during the first year. In the latter series, 85 occurred in the second to the fourteenth year, and 59 after that time.

**The Location of Intussusception.**—The agonal invaginations are usually found in the small intestines. Pathological intussusception may occupy any part of the intestinal tract, but much more commonly originates at the ileocecal valve than at any other point. In the majority of cases, especially in childhood, the ileocecal valve prolapses into the cecum and thus becomes the apex of the intussusceptum, dragging the ileum after it. The cecum and colon form the outer and middle layer, the ileum the inner. The term ileocecal intussusception is applied to such cases. Less frequently the ileum prolapses through the valve into the colon and is carried farther on. The name ileocolic is given to this form, which is certainly rare. Leichtenstern found, in an analysis of cases at all ages, that invagination of the small into the large bowel occurred in 52 per cent., iliac intussusception in 30 per cent., and colic in 18 per cent. In adults the iliac and the ileocecal varieties were of approximately equal frequency. Other large series have shown about similar proportions; but in small groups of cases great variations have naturally been encountered.

**Pathology.**—Secondary changes take place in the intussusception, according to the degree of constriction at the neck. There is practically always more or less interruption of the circulation in the mesentery entering into the invagination, and a consequent intense congestion of the intussusceptum. This becomes dark red, purplish, or blackish, and is swollen as the result of the hyperemia and attendant œdema. Ecchymotic hemorrhages occur within the bowel wall, and exudation of hemorrhagic fluid into the lumen of the bowel takes place. The most marked change occurs in the middle layer of the invagination.

In the later stages, when the swelling of the invaginated portion has become extreme, complete obstruction of the lumen of the bowel occurs, and at the same time an increase of circulatory interference with resulting gangrene. In acute cases this may develop as early as the end of the first day; although it is usually not met with, even in the acute cases, before the expiration of three or four days. In the chronic cases gangrenous changes may be delayed for a long time, sometimes not appearing until a number of months after the onset. The gangrene usually first affects the apex of the intussusception, but in other instances it begins at the neck. As the result of the gangrenous necrosis, portions of sloughed-off bowel may be passed from the rectum.

Peritonitis affecting the enfolded portion of the serous covering of the bowel (that is, the serous coat of the innermost and middle reflection of the bowel, where they lie in contact) sets in rather promptly; usually becoming marked by the end of the second or third day. This may be confined to the region of the neck of the invagination, or may be extensive, and involve the entire serous coating within the sac. The invaginated portions become agglutinated, and reduction of the intussusception is more difficult. In the late stages, especially in the chronic cases, firm adhesions may form between the two layers of peritoneum adjacent to



one another. When such adhesions have formed at the neck of the sac, and the intussusceptum has been discharged after sloughing or gangrene, relief may occur. More commonly a stenosis of the bowel results from cicatrization, and a partial intestinal obstruction, which later may become complete, is the terminal condition.

**Symptoms.**—The symptomatology varies widely, some cases being comparatively slow in development and chronic in course, and others highly acute in onset and terminating rapidly. In the great majority the onset is sudden and occurs without any apparent predisposing condition. Sudden violent pain of a cramp-like character usually initiates the disease, and is speedily followed by nausea and vomiting. In many instances tenesmus and one or more movements of the bowels follow, and sometimes a diarrhœal condition sets in. The movements may be composed of mucus alone, of mucus mixed with blood or of pure blood. The degree of tenesmus and of diarrhœa depends to some extent upon the situation of the intussusception, being more marked when this involves the lower portion of the bowel or the rectum.

Distension of the abdomen may appear, but is not, as a rule, a marked condition. Direct physical examination discloses a palpable tumor in many cases. This is usually felt in the left side of the abdomen, when the intussusception has become extensive and has reached that point. The tumor may, however, be felt at the ileocecal region, where the intussusception, as a rule, begins. It is usually elongated, cylindrical, or sausage-shaped. Contractions of the bowel ensheathing the invaginated portion may cause a change in the consistency as well as in the size of the mass. Occasionally an intussusception extends so far as to protrude through the anus. In chronic or slowly developing cases the tumor may be found to change its position, moving in the direction of the intestinal tract.

In the acute cases, after an onset of this character, symptoms of depression and collapse occur, usually within from one to three days. At the same time the vomiting, as in other cases of intestinal obstruction, becomes fecal in character. In chronic cases, if the onset has been acute, the symptoms gradually subside and may become relatively inconspicuous. In other cases, the clinical course is of a chronic character.

The most important symptoms are the pain, the tumor, and the peculiar behavior of the bowels. The *pain* in the early stages may be intense—so severe, indeed, that it occasions collapse. This is particularly marked in the acute forms in early childhood. Later, paroxysms of colicky pain recur from time to time, with more or less frequency. Attending this there may be a tonic contraction or stiffening of the segment of the intestine above the point of intussusception, and in other cases of intestinal obstruction. *Tenesmus* is more frequently met with in this form of intestinal obstruction than in any other; it is earlier in its appearance, and more intense the nearer the invagination approaches the rectum. The character of the stools is a highly important diagnostic indication. There may at first be a discharge of fecal matter from the lower bowel, but soon the movements, if they continue, become mucous, bloody, or of mixed mucus and blood, while the discharge of fecal matter

ceases. The evacuations may be attended with sharp recurrences of the characteristic tenesmus. Sometimes large hemorrhagic movements or actual hemorrhages may occur.

**Prognosis.**—The termination of intussusception varies greatly. A rapid course with a fatal termination is more frequent in infants than in the intussusception of later life. Subacute and chronic cases, running a course of weeks or even months, occur as a rule in the older subjects. Even in these, however, the eventual termination is usually fatal. Reference has been made to occasional spontaneous cures; but, taking the number of these in large series, this outcome is exceedingly rare. Occasionally complete cure by spontaneous or induced disinvagination may take place in cases in which peritonitis and adhesions have not developed or have been so slight that the invaginated portion was able to escape. A few instances have been met with in which such relief occurred after the condition had persisted for a considerable time.

**Treatment.**—In cases of intussusception recognized early, and especially in infants, manipulation combined with enemata may effect relief in a considerable proportion of instances. The mass is grasped in the fingers of one hand (the patient being anesthetized) and gentle traction made with the other hand in a direction to effect disinvagination, or pressure is made against the apex of the invagination to cause its release. Following this, or between the efforts of manual relief, enemata of water (from  $\frac{1}{2}$  liter in children to 2 liters in adults) may be allowed to flow into the rectum through a soft rubber tube and under a pressure of four or five feet, great care being taken to lower the funnel should undue distension seem to occur in the lower bowel. In adults these methods of treatment are less often satisfactory. In them as well as in infants, if the simpler plan of treatment has failed, surgical treatment must be adopted before too long a time has elapsed.

**Volvulus.**—This term is applied to various kinds of twisting, knotting, or rotation of segments of bowel, resulting in partial or complete obstruction. A loop of intestine may become obstructed by rotating about its mesenteric attachment, which acts as a sort of pedicle; in other cases volvulus is due to a twisting or rotation of the bowel on its own longitudinal axis, while in still other cases one loop of intestine twines about the mesenteric attachment of another, or intertwining may take place between two or several coils.

**Etiology.**—Abnormal length of the mesenteric attachment of a loop of bowel, especially when combined with a lateral contraction of the mesentery, is the most important cause of volvulus. The mesentery may be elongated congenitally or it may become stretched as a result of continued constipation and overloading of the affected portion of the bowel, and some stretching may result from adhesions of some part of the intestinal canal to fixed abdominal structures. A not uncommon cause of elongation is the inclusion of a coil of intestine in a hernial sac. Narrowing or contraction of the mesentery may occur without special elongation as a result of inflammatory conditions. A laxness and relative elongation of the mesentery may be caused by a loss of fat

in the abdominal walls and in the mesentery itself. In women, after repeated pregnancy, these conditions frequently occur.

The conditions which predispose to volvulus are more frequently found in persons of advanced years than in the young, and volvulus is therefore most common in the aged or those past middle life. The immediate cause may be a strain or some effort, as in lifting, or a traumatism, such as in compression of the body. Sometimes overloading of the intestinal tract combined with some effort or strain is of importance. Thus in old people who have suffered from habitual constipation the sigmoid flexure becomes elongated and its mesentery stretched.

**Pathology.**—In simple volvulus, a loop of intestine twists about its mesenteric attachment. There may be a partial turn or several complete turns. In the former case the obstruction of the bowel is partial or incomplete; in the latter it is almost certainly complete, and in addition the bloodvessels become so compressed that intense venous engorgement results. Whether the obstruction is partial or complete, but especially in the latter case, distension of the obstructed portion of the bowel rapidly ensues. The bowel becomes dark red or purplish in color, and its walls are deeply engorged with blood and swollen by œdema. Then extravasations of blood are seen upon the surface and blood-stained liquid exudes into the lumen of the bowel as well as into the peritoneal cavity. Finally gangrene takes place. The striæ of the bowel are obliterated by the overextension, and rents of the serous coat may occur. Rupture of the bowel, however, rarely takes place. It is more likely to be found above the volvulus than in the affected portion.

Peritonitis sets in rather promptly as a result of the escape of bacteria through the injured, congested, and œdematous walls of the bowel. When bloody extravasation is present in the peritoneal cavity the escaping bacteria may occasion putrefactive changes.

**Seats.**—Volvulus most frequently involves the sigmoid flexure, but may occur at the junction of the small and large intestine or in some portion of the small intestine. In volvulus of the sigmoid there is usually a simple rotation of the flexure about its mesenteric attachment. The rotation is usually in such a direction that the rectum is carried posteriorly to the descending colon, but sometimes the twist is in the opposite direction, so that the rectum is carried forward and lies in front. Occasionally the sigmoid may become coiled about a loop of the small intestine or about the pedicle of a pelvic or abdominal tumor.

Volvulus at the junction of the small and large intestine usually involves both the ileum and colon and is occasioned by an abnormal length of mesentery. Simple rotation of the colon on its own axis has been described, but is probably rare.

Volvulus of the small intestine resembles that of the sigmoid. Rarely two or more loops may be intertwined. Unusual length of the mesentery is the ordinary cause; but some other pathological condition, such as the passage of a loop of the bowel through an internal hernial orifice or under a band, may be the direct cause of the volvulus. In these conditions the loop of bowel after incarceration becomes twisted upon itself at the point where it is engaged in the hernial opening or under a band. A foreign body within the bowel may occasion the twist.



**Symptoms.**—These are usually those of an acute intestinal obstruction. When the obstruction is only partial in the beginning, there may be a subacute onset which goes on to complete obstruction as the volvulus increases. The symptoms vary according to the location of the lesion. In volvulus of the sigmoid there is usually sudden severe pain followed by paroxysms of cramp or colic, and, as a rule, by absolute constipation. Reflex disturbances, such as vomiting, are often wanting because of the low situation of the obstruction. Sometimes, instead of constipation, there is a tendency to mucous discharges with tenesmus, and occasionally ordinary diarrhoea may occur. The abdomen soon becomes intensely tender and enormously distended. The superaddition of peritonitis, which usually occurs within twenty-four to forty-eight hours, causes increased tenderness and swelling and adds greatly to the prostration.

In volvulus affecting other portions of the intestine the symptoms are similar; vomiting is more conspicuous, especially in cases in which the small intestine is involved in its upper portions. In all cases the distension of the coil of the bowel included in the volvulus causes a localized tumefaction, which may be so hard that it simulates a solid mass. The situation of this may indicate the location of the volvulus, although it must be remembered that the length and mobility of a cecum and even of the sigmoid may readily cause confusion.

**Prognosis.**—This is usually very grave. In some instances the condition relieves itself spontaneously. This is probably more common in the case of the small intestine, but certainly occurs even when the sigmoid is involved. Usually, unless speedily relieved by surgical means, localized peritonitis and gangrene of the involved area soon take place, and death speedily follows.

**Differential Diagnosis of the Conditions Causing Obstruction.**—It is often impossible to distinguish between the different causes of acute or chronic obstruction, although sometimes antecedent conditions, the manner of development of the symptoms, and the clinical course may furnish fairly reliable evidence of the nature of the condition.

Among *foreign bodies* the most common cause of obstruction is gall-stones. When a biliary calculus enters the duodenum and causes obstruction, the vomiting and prostration at once reach grades of the highest severity. Relief may follow the dislodgement of the stone and its transportation to lower levels but if it remains high up, early fecal vomiting and collapse usually result. A preceding history of gall-stones and jaundice or other significant symptoms may make the diagnosis fairly certain.

Obstruction by *bands* usually involves some portion of the small intestine and causes symptoms of a decidedly acute character, with early development of fecal vomiting, prostration, etc. Internal hernia also involves the small intestine, and cannot usually be distinguished with accuracy from the former.

*Intussusception* usually involves the ileum or the ileum and cecum, and is more frequently found in childhood or early life than at or after maturity. The symptoms of onset are decidedly less acute than in obstruction of the small bowel by bands. Localization of the place of obstruction is sometimes readily made by the situation of the pain,

the development of a local tumefaction, and the situation of stiffening or tonic contraction of the bowel. The localization of the obstruction, the discovery of a sausage-shaped tumor, the characteristic stools, and especially the occurrence in childhood may establish the diagnosis. In acute cases, however, especially those occurring in young infants, the intense pain and sudden collapse may mask other indications, and the nature of the condition may be difficult to determine.

*Volvulus* usually involves the sigmoid flexure, and occurs in persons of somewhat advanced years, and especially in the aged. The symptoms are slow in development and often inconspicuous until a late stage in the disease. The localization of the point of obstruction may often be established, although sometimes a redundant sigmoid may occasion confusion. Strictures and partial obstructions of the bowel may be suggested by the occasional occurrence of attacks of abdominal distension, with relief after active movements of flatus.

Obstruction by carcinoma and other tumors usually occurs in the large bowel. Although tumors in their general relations are considered elsewhere, some of the features that indicate a neoplasm as the cause of intestinal obstruction may be appropriately referred to in this place. Attacks of distension with active peristalsis and movements of flatus may occur from time to time, followed by more severe seizures, marked by violent abdominal colic. In these cases the patient himself may be able to recognize the point of obstruction by feeling the place of spasmodic contraction above the lesion. On palpation the physician may discover a hardening which appears at a certain place, and after a moment or two or a longer period of time relaxes. When the growth is situated favorably for palpation, or has reached considerable size, it may be discovered on abdominal palpation. When situated in the rectum, a digital rectal examination or the enteroscope may disclose its presence. As in other forms of obstruction involving the large bowel, the passage of stools of characteristic form some time before complete obstruction has developed and the occurrence of mucous, mucopurulent and blood-streaked or bloody passage may aid. Bloody and mucous movements are more frequent in carcinomatous obstruction than in any other form.

Obstructions due to fecal accumulation rarely occur independently of other causes of obstruction, except when the accumulation takes place in the rectum as the result of habitual constipation. In these cases the development of the condition is so gradual that the existence of obstruction may not manifest itself until, more or less suddenly, after the upper bowel has exhausted itself in efforts to maintain the onward movement of its contents, sudden paralysis takes place. In the earlier stages the most characteristic indication is the increasing difficulty of securing evacuations and the insufficiency of these. With this there may be a gradual increase in abdominal girth from general meteorism; and on careful palpation the colon throughout its length may be found distended beyond normal dimensions. Hardened masses may also be discovered in the left iliac region, or, on digital examination, in the rectum. If the abdominal walls are thin and the peristalsis maintains itself actively, visible peristalsis may be seen for some time before the degree

of contractions and the grade of obstruction cause sharp attacks of colic. In many instances of gradually developing impaction, fairly regular movements, seemingly adequate in quantity, may occur for some time after the onset. Still more puzzling are the cases in which a continuous diarrhoea is maintained as the result of catarrhal inflammation of the bowel by retained fecal masses. A similar condition occurs in some instances of carcinoma of the lower bowel.

**Prognosis.**—The termination of intestinal obstruction depends upon the nature of the obstruction and its completeness. In acute occlusions that cannot be relieved death may occur within a few hours, or not until several or many days have elapsed. Leichtenstern estimates the average duration at six days. Partial or chronic obstructions may persist for very long periods of time; in some cases for years. Repeated vomiting, excessive shock, prostration, and collapse are the usual conditions that precede death in acute cases; the persistence of such conditions is, therefore, a prognostic indication of great gravity. Another cause of death in acute cases is peritonitis. In cases of greater duration, toxic manifestations usually set in before death ensues.

Recovery from intestinal obstruction may occur spontaneously in cases of fecal impaction or compression of the bowel; and sometimes in cases in which the obstruction is due to adhesions, bands, internal hernia, or the presence of foreign bodies within the bowel. In intussusception, spontaneous disinvagination may occur, or the intussusceptum may slough off and recovery may take place; while in volvulus the twisted loop of bowel may be spontaneously restored to its normal condition. A recurrence of obstruction after a primary relief sometimes takes place.

**Treatment.**—Practically all forms of intestinal obstruction demand surgical treatment. In cases of partial obstruction, however, and in some conditions like impaction of feces or the presence of foreign bodies within the bowel, medical treatment deserves a careful trial. In the early stages, before an absolute diagnosis of obstruction has been made and before surgical intervention can properly be advised, certain indications must be met by medical means. In cases, however, in which it has thought well to institute medical treatment, this form of management should not be persisted in longer than a day or two, if relief of the obstruction is not apparent. It is far better to err on the side of too early operation than the reverse; and in all cases of doubt, surgical rather than medical measures should be adopted.

In the beginning the patient should be placed at as complete rest as possible, and the diet should be restricted or completely withheld even if marked gastric disturbances are not present. Small particles of ice may be allowed to quench thirst; but the unrestricted use of ice may occasion disturbance of the stomach and is objectionable. Enemata of water and hypodermic injections of saline solutions may be given.

The use of laxatives must be condemned, except in certain special conditions. If they are effective at all in stimulating peristalsis, they will increase, instead of relieve, the abnormal conditions. Fortunately, when administered in error of diagnosis, vomiting usually causes their prompt expulsion. In fecal impaction purgatives are often desirable,



although they must be employed with caution. Small doses of calomel or salines are preferable to more active remedies, because they produce serous outpourings without stimulating violent peristalsis. In cases of partial occlusion the accumulation of feces may be prevented by the occasional use of the same or other laxative remedies.

Enemata and colonic flushings are specially advisable in cases of obstruction due to fecal impaction. The repeated use of warm water, saline solutions, or oil may break up an impaction that threatens to cause complete obstruction. The injections must be given cautiously and without undue force, as the irritation caused by them may stimulate violent peristalsis above the point of obstruction. The same plan of treatment is sometimes effectual in dislodging a foreign body; but the use of forced injections of fluids in cases of intussusception, volvulus, etc., cannot be too strongly condemned. Formerly inflation of the bowel with atmospheric air or various gases was practised for the relief of intussusception and other kinds of organic obstruction. This method also merits condemnation.

Opium and atropine are administered with advantage in some cases of obstruction for the purpose of quieting spasm or excessive peristaltic efforts. Thus in cases of internal hernia or occlusion by bands the obstruction may become more complete as the result of the violent peristalsis stimulated at the point of occlusion. Complete rest, the use of poultices or other warm applications, and small doses of opium or atropine, may relieve active peristalsis; and a release of the incarcerated bowel may take place, although this can rarely be hoped for. Similarly in cases of obstruction by foreign bodies the same remedies, especially atropine, may aid in relaxing spasm and thus facilitate the passage of the occluding body. Besides these indications, opium or morphine is sometimes necessary, even though operation is decided on to control the pain. The doses should be no greater than are required to allay suffering; and, generally speaking, hypodermic injections are preferable to administration by the mouth or by the rectum.

External treatment to the abdomen may be useful in cases of obstruction which can be relieved, such as those due to foreign bodies or impaction, and some cases of incarceration by bands, through slits, etc. Large poultices or warm fomentations of various sorts may be used for this purpose. Even though ineffectual in accomplishing a relief of the obstruction, such applications frequently give comfort. Massage of the abdomen is particularly helpful in cases of partial obstruction, such as are caused by adhesions after operations, or those due to the presence of foreign bodies. After relief from impaction in cases of narrowing of the lumen of the bowel, subsequent accumulations may be prevented by systematic manipulations combined with the administration of laxatives and the injection of warm saline solution or oil into the bowel. In acute obstruction, external manipulations must be used with the greatest caution.

Certain symptoms may require treatment before or after operation has been decided on. Among these, gastric disturbances are most important. Nausea and vomiting may greatly complicate the difficulties

under which the patient labors and contribute largely to prostration. When laxatives are permissible, small doses of calomel placed upon the tongue may have a controlling effect. When the disturbance of the stomach is more intense, lavage of the stomach is advisable. If resorted to early, this method of treatment may reduce subsequent difficulties materially. Sometimes an actual cure of obstruction has been obtained from gastric lavage, as Kussmaul, who introduced this method of treatment, first pointed out. Surgeons quite uniformly recommend lavage as being useful in allaying the danger from subsequent anesthesia, when vomited material so readily gains access to the lungs. If used at all, lavage should be resorted to in the early stages.

**Surgical Treatment.**—In all cases of obstruction in which the symptoms are not relieved within forty-eight hours under general and medical management, surgical intervention must be advised, and in many cases immediate operation should be recommended. Attempts to relieve volvulus and complete obstructions by bands and the like by means other than surgical operation are inadvisable, although occasional cures have been obtained from such treatment. In the long run, the loss of time and strength thus occasioned makes the subsequent operative measures less likely to prove successful.

### VOLVULUS OF THE OMENTUM

Volvulus of the omentum may be considered briefly in this place on account of the resemblance of the symptoms to those of intestinal obstruction. The great omentum may become twisted in the same manner as a coil of intestine. This usually takes place either in a part of the omentum included in a hernia or in a contracted portion that had been contained in a hernia and afterward restored to the abdominal cavity. Sometimes the twisting is the result of adhesions of the omentum to fixed structures. Occasionally several turns are observed, and some of these may be manifestly of considerable duration.

The omentum becomes swollen, oedematous, engorged with blood, and finally may undergo necrotic change from stasis. Hemorrhagic extravasations into its tissues and free exudation or extravasation into the abdominal cavity may take place.

**Symptoms.**—These are similar to those of intestinal obstruction. Sudden and severe abdominal pain with nausea and vomiting are the initial manifestations. The appearance of an abdominal mass, more or less tender on pressure, or the sudden distension of a hernial sac, if the twisted omentum is contained within the sac, are usually met with. Constipation is usually present but is less obstinate than in cases of volvulus of the bowel.

*Treatment* is purely surgical.

### INTESTINAL OBSTRUCTION DUE TO MOTOR PARALYSIS

Partial or complete obstruction may be due to motor insufficiency or complete paralysis of the motor power of the bowel. Sometimes

this results from direct or reflex causes without organic lesions affecting the bowel itself. More frequently such obstruction from paralysis is a concomitant of organic diseases of the bowel.

**Functional Paralysis.**—A complete paralytic obstruction has occasionally been observed as the result of injuries or diseased conditions, such as contusion, compression, or torsion of the ovary or testicle, various inflammatory conditions in the inguinal region or in hernial sacs, after operations for hemorrhoids, or in consequence of the passage of renal or biliary calculi. In such cases the paralysis of the bowel is a result of violent irritation of the sensory nervous mechanisms.

Cases have been observed in which the condition has followed paracentesis of large abdominal effusions or injuries to the abdominal cavity of various sorts, not involving the viscera. In a similar manner, after abdominal operations in which the intestines have not been involved, and in which infection of the peritoneum has not been discoverable, a paralytic condition of the bowel has developed.

After the reduction of hernias, paralysis of the affected coils may occur, although the bowel presents no evidence of inflammatory or other organic change. In cases of intestinal obstruction involving the upper part of the small intestine, complete cessation of all movements indicates a secondary paralytic condition of the lower bowel. In all these cases there is a functional paralysis which may be explained by a direct or reflex stimulation of the inhibitory nerve, the splanchnic, which occasions cessation of peristaltic movements.

In another group of cases the paralytic condition is probably due to toxic conditions affecting the intestinal walls or the nervous mechanism of peristalsis. In this group may be included the occasional cases of paralysis of the bowel occurring in the course of severe attacks of pleurisy or pneumonia. Mannaberg and the writer have observed instances of this sort. In some cases the obstruction was so severe as to call for operation. A similar condition occasionally attends cases of cholera, typhoid fever, and severe intestinal intoxications or enteritis. In all these instances the absorption of toxic matters acting upon the muscles or upon the nervous apparatus may explain the condition.

**Paralysis of the Bowel Attending Organic Disease.**—Much more common than the preceding are the cases in which segments or a large part of the intestinal canal become obstructed by paralysis that is secondary to some form of intense organic disease. The more frequent and important cause of such paralysis is acute peritonitis. In cases of general peritonitis the bowel soon becomes quiescent; finally, all peristalsis ceases and a paralytic condition ensues. In localized peritonitis, such as that attending appendicitis, localized segments are involved. In chronic peritonitis and tuberculous peritonitis, obstruction of the bowel is more commonly due to adhesions or mechanical obstructions, although the inflammation of the bowel wall and the reflex nervous influences also play a part in the process. Embolism and thrombosis of the mesenteric vessels occasion a paralysis and consequent obstruction. In all those cases in which paralysis has followed organic lesions the cause of the motor palsy is in part the direct involvement of the wall



of the intestine in the disease process, and in part the effect of this condition upon the nervous apparatus.

Occasionally paralysis is due to excessive accumulations of intestinal gases or of fecal matter. In cases of chronic constipation or partial obstruction of the bowel, or in various diseases in which a partial but not a complete paralysis has occurred, excessive meteorism may determine a complete paralysis; or the gradual accumulation of fecal matter may so distend the bowel as to cause the complete cessation of all peristaltic power.

**Symptoms.**—The symptoms are practically those of obstruction by mechanical causes. When due to violent reflex nervous stimuli, as in cases of injury to the ovary or testicle, or to the passage of calculi, the onset may be attended with sudden intense pain, vomiting, and prostration, following which obstinate constipation and distension of the abdomen make their appearance. Although vomiting is usually marked, it less commonly becomes fecal in character than in cases of mechanical obstruction. Other symptoms may indicate the cause of the paralytic condition, and may serve to establish a correct diagnosis; although this is usually difficult. The course depends upon the cause. In cases in which some injury has occasioned the paralysis, a return to normal conditions may occur after the original disease has subsided. Paresis of the bowel following operations, and that attending peritonitis, whether local or general, are exceedingly grave conditions.

**Treatment.**—This must always be directed to the original cause of the intestinal condition. Sometimes this may be controlled by medical means, as in toxic or inflammatory conditions of the bowels; in other cases, as when an injury has been sustained, local applications or cold or other local measures may be employed with advantage. Surgical intervention is frequently necessary. Moderate paralytic conditions of the bowel may sometimes be corrected by hypodermic injections of sulphate of eserine (gr.  $\frac{1}{100}$  to gr.  $\frac{1}{50}$ ); by colonic douches of cool water or saline solution, or enemata containing stimulating remedies like asafetida and turpentine. External applications, such as mustard plasters and turpentine stupes, may also be beneficial. In cases of paralysis of the bowel following other abdominal diseases, surgical treatment of the original condition alone can be relied upon.

### INTESTINAL DIVERTICULA

Intestinal diverticula are classified as congenital and acquired. According to their anatomical peculiarities they can be divided into true and false diverticula. *True* diverticula are those composed of all the coats of the normal intestinal wall. *False* diverticula are those composed of only the mucosa and serosa. They are, in other words, hernial protrusions of the mucosa through defects in the muscularis. As most congenital diverticula are true and most acquired are false, the terms "congenital" and "true" and "acquired" and "false" have often been employed synonymously. Although in the majority of cases this holds good,

some cases of the acquired form have apparently been true diverticula, so that the synonymous use of the terms "acquired" and "false" is not to be recommended.

**Congenital Diverticula.**—Meckel's diverticulum, so called, is the only form of congenital diverticulum that requires description. Other forms are of such extreme rarity as to be of no practical significance. Meckel's diverticulum results from the persistence of the omphalo-mesenteric duct. This should be entirely obliterated by the sixth or seventh week of fetal life, but some remains of it are frequently found. It is apparently more common in males than in females. Kelynack found 4 cases of Meckel's diverticulum in 298 autopsies, all 4 cases occurring in males, while in 337 cases Rolleston found 10 instances, 9 of which were in males. The diverticulum usually takes its origin from the convex side of the small intestine, about 1 meter above the ileocecal valve. Exceptionally it arises from the upper portion of the small intestine. It varies from 3 to 10 cm. in length and may be as long as 25 cm. The wall of the diverticulum, commonly composed of the same structures as the intestinal wall, and its mucosa contain both Lieberkühn's glands and Peyer's patches. The lumen of the intestinal end of the diverticulum is large, frequently as large as that of the intestine itself. A valve-like fold of the mucous membrane at times occludes the opening of the diverticulum. Toward the free end of the diverticulum the lumen decreases, so that the process has something of a conical form. Occasionally the end is enlarged, at times assuming a hammer-like form. In unusual cases the same lumen is maintained throughout the entire extent of the diverticulum.

Usually the end lies free within the abdominal cavity. Occasionally, however, it remains attached to the umbilicus. Under these circumstances the lumen of the peripheral end alone becomes obliterated, forming a fibrous cord, but in other cases the entire duct may remain patulous, thus forming a free communication between the external surface and the ileum, permitting the discharge of intestinal contents at the umbilicus. Hubbard has collected 9 such cases, in all of which operation resulted in a cure. The remains of the duct in the umbilicus may give rise to an adenomatous growth or carcinoma.

When, as is usually the case, the peripheral portion of the lumen becomes obliterated, the fibrous cord resulting may remain attached to the umbilicus and later become the possible cause of intestinal strangulation, or this cord may atrophy, and the end of the diverticulum then becomes free within the abdominal cavity. Subsequently inflammatory conditions may cause the free end to become adherent to any point within the abdominal cavity with which it may come in contact. This is most frequently the mesentery. Cazin and Halstead<sup>1</sup> have made exhaustive analyses of the various places and structures to which the peripheral end of Meckel's diverticulum may attach itself, and Fitz<sup>2</sup> discussed the possibilities of strangulation of portions of the intestinal tract by such adherent diverticula.

<sup>1</sup> Halstead, *Annals of Surgery*, 1902, xxxv, 471.

<sup>2</sup> *Amer. Jour. Med. Sci.*, 1884, lxxxviii, 30.

If, finally, the diverticulum assumes its most frequent form, a finger-like projection, the tip of which lies free within the abdominal cavity, it may remain an entirely harmless appendage throughout the patient's life. On the other hand, it may be the seat of various phenomena of extreme gravity. It may be the seat of a volvulus by rotating upon its own axis; it may be the starting-point of an intussusception by becoming inverted into the ileum; or it may become knotted about a coil of intestines and produce stricture. If, as is sometimes the case, the diverticulum possesses a mesentery of its own, the latter may produce a stricture of the ileum. Occasionally the lumen becomes occluded at its intestinal end, inducing cyst formation which may suppurate or by pressure produce obstruction of the intestines. Ulcerations of the mucosa of the diverticulum, sometimes perforative, may result from fecal accumulations or from typhoid or tuberculous infection.

**Acquired Diverticula.**—These may be true or false. True acquired diverticula are of extreme rarity. They are usually in the form of minute spherical or conical traction diverticula, occurring as a result of adhesions due to some extra-intestinal inflammatory condition. It appears possible, however, to have a true acquired diverticulum which is not the result of traction. Such a condition appears to have been present in the first case reported by Mayo, Wilson, and Giffin.<sup>1</sup> False diverticula are hernial protrusions of the mucous coat through the muscular coat. As the protrusion of the mucous coat makes its way through the muscular coat it naturally carries the serosa with it, so that usually the wall of the diverticulum is composed of mucosa and serosa. At times a few muscular fibres are found between the two layers. These diverticula may be conical, cylindrical, hemispherical, or irregularly lobulated, and vary in size from that of a pea to that of an apple. They may occur throughout the entire intestinal tract, but are more frequently found in the large than in the small intestine. As a rule, they are multiple, and at times occur in extraordinary numbers. Hansemann has recorded as many as 400 in a case. They differ from Meckel's diverticulum in that they usually arise from the concave side of the intestine close to the mesenteric attachment. At times they occur between the peritoneal coats of the mesentery. It has been claimed that the simple intra-intestinal pressure resulting from long-continued constipation is the etiological factor. Another view is that they result from the atrophy of some of the fibrous elements of the intestinal wall. A view that at the present day has many adherents is that first advanced by Klebs, namely, that the point of entrance of the mesenteric vessels into the intestinal wall forms a focus of lessened resistance through which the mucosa forces itself, carrying with it the overlying serosa. The primary factor in the production of diverticula is decreased resistance of the intestinal wall. This may be due to structural weakness at the points of entrance of the vessels or to areas of atrophy of the fibrous or muscular tissues of the bowel wall. The various theories of the production of intestinal diverticula are thoroughly discussed by Fischer.<sup>2</sup>

<sup>1</sup> *Transactions of the American Surgical Association*, 1907, p. 240.

<sup>2</sup> *Jour. Exper. Med.*, 1901, v, 333.



According to Gordinier and Sampson, acquired diverticula were found 64 times in 8132 autopsies (Dresden Hospital); 19 times in 2600 autopsies (Johns Hopkins Hospital); twice in 953 autopsies (Bender Hygienic Laboratory); once in 2382 autopsies (Boston City Hospital). Careful investigation of left-sided tumors will doubtless reveal more.

Retention of fecal matter and infection may occasion inflammatory lesions of the mucous lining or entire wall of the diverticulum and localized peritonitis, sometimes with considerable induration, may surround the diverticulum and involve the adjacent portions of the bowel wall. Tumors of considerable size and easily palpated through the abdominal wall may result. In cases of inflammation confined to the mucosa, ulceration and perforation into the peritoneal cavity may occur, sometimes quite acutely. In the case of the tumor-like indurations surrounding the diverticulum intestinal obstruction is more frequently the consequence. The term "diverticulitis" may be applied to both classes.

A variety of diverticula requiring special mention are those occurring in the duodenum at the site of the papilla of Vater. They are apparently due to weakening of the intestinal wall at the point of entrance of the bile-duct. Keith claims that they occur in women from a forced visceroptosis, as the result of the pressure of corsets. The forced descent of the duodenum is not participated in by the bile or pancreatic ducts, on account of their more fibrous consistency, and a pouching of the intestinal wall in the neighborhood of the papilla thus results.

Bland-Sutton<sup>1</sup> describes a form of abscess of the epiploic appendages caused by the penetration of foreign bodies through the intestinal wall and their lodgement in the epiploic appendage. Anatomically the appendix epiploica is a fold of peritoneum filled with fat, the latter being directly continuous with the subserous fat of the intestine. Very often after middle life there appear in the wall of the gut, especially of the descending colon, small pouch-like diverticula in which small foreign bodies may lodge and so penetrate the intestinal wall. In thin individuals the foreign body would probably enter the peritoneal cavity, while in the more obese it might enter the epiploic appendage and set up an inflammatory disturbance.

In a large majority of cases acquired diverticula give no clinical evidence of their existence. Lately, however, those situated in the descending colon, and especially in the sigmoid flexure, have been shown to be the cause of very profound diseased conditions, and their recognition explains some obscure phenomena having their seat in the left iliac fossa. Among the contributions which have shed light upon the condition are those of Mayo, Wilson, and Griffin, Brewer,<sup>2</sup> and Beer.<sup>3</sup>

The *clinical features* presented by these cases may conveniently be divided into the inflammatory and the obstructive.

The *inflammatory* phenomena may be the result of either a virulent infection of the diverticulum or perforation. The symptoms may briefly be described as those of appendicitis on the left side. The patients are

<sup>1</sup> *The Lancet*, 1903, ii, 1148.

<sup>2</sup> *Trans. Amer. Surg. Assoc.*, 1907, p. 258.

<sup>3</sup> *Amer. Jour. Med. Sci.*, 1904, cxviii, 135.

usually males over forty-five years of age, otherwise in robust health, and generally inclining to obesity. The direct attack may be preceded by left-sided pain low in the abdomen, coming in spells and associated with constipation. Sudden, more acute pain, general at first, later localized to the left iliac fossa, and more or less paroxysmal in type, marks the onset of definite symptoms. Vomiting is usually not marked unless the pain is very severe. There is more or less rigidity of the left rectus muscle. The previous constipation may now change to diarrhoea. Finally a mass is discovered developing to the left of the median line in the middle or lower quadrant of the abdomen. In women this mass is at times pelvic rather than abdominal.

In the *obstructive* cases the inflammatory symptoms are much less marked and the general symptoms of slowly progressive obstruction predominate. The condition may be readily confounded with carcinoma, especially as both conditions occur in advanced life; the formation of the tumor is, however, more rapid in the former. In diverticular obstruction there is usually a noticeable disharmony between the rather considerable size of the tumor and the lack of cachexia. Furthermore, the presence of blood in the stools would point strongly in favor of carcinoma.

The *treatment* of all forms of diverticula is purely surgical.

### CARCINOMA OF THE INTESTINES

Compiling the statistics of Maydl, Nothnagel, Heimann, Zemann, and Müller, we find that of 26,340 cases of carcinoma in general, 2255, or 8.56 per cent., were in some portion of the intestines inclusive of the rectum. In determining the location of the tumor in the intestines there is a marked predominance of carcinoma of the colon and rectum. Combining the statistics of Maydl, Nothnagel, Zemann, Müller and Bryant, it is seen that of the 659 instances of intestinal carcinoma that they have collected, 6.22 per cent. were in the small intestines, 6.82 per cent. in the cecum and appendix, 22.76 per cent. in the various portions of the colon, and 64.18 per cent. in the sigmoid and rectum. Carcinoma of the duodenum is frequent as compared with the ileum and jejunum, despite the great difference in the lengths. In the combined statistics of Maydl, Nothnagel, and Müller, of the 26 cases of carcinoma of the small intestine, 13 were in the duodenum and the remaining 13 in the ileum and jejunum. Rolleston collected 54 cases of primary cancer of the duodenum and but 19 of the jejunum and ileum.

Carcinoma of the intestine is in the vast majority of cases primary. Secondary involvement may occur either by metastasis or by direct extension. Metastatic involvement is seldom noted, and when it does occur it is not infrequently as a part of a general carcinomatosis. Metastatic carcinoma of the intestines is usually multiple. The nodules have a tendency to locate in the mesentery just at its attachment to the intestines, thus producing multiple stenoses without involvement of the mucosa. Direct extension of cancer of a neighboring organ to the intestines is somewhat more common and occurs especially as a result of carcinoma of the pancreas, gall ducts, and pelvic viscera.

*Sex* is of little etiological significance in cancer of the intestines. Males are apparently somewhat more frequently affected with carcinoma of the rectum and sigmoid, whereas this relative susceptibility is less evident in carcinoma of the upper portion of the tract. *Age* is probably a less important factor in carcinoma of the intestines than in carcinoma of almost any other portion of the body. The majority of cases occur in individuals over forty years of age, but not infrequently the condition is found in younger individuals. According to Maydl, one-sixth of all cases of carcinoma of the intestines occur between thirty and forty years of age, and one-seventh under thirty years of age. Bernoulli has collected 37 cases in individuals under thirty years of age, and Nothnagel mentions 8 cases in individuals under twenty years of age. One of them was in a three-year-old boy, another in a boy aged three and a half years.

**Pathology.**—The majority of intestinal carcinomata are cylinder-celled adenocarcinomata taking their origin from the intestinal glands. Depending upon the relative proportions of the connective tissue to the epithelial elements, these tumors may be simple, medullary, or scirrhus. Of somewhat less frequent occurrence than cylinder-celled adenocarcinomata are cylinder-celled solid carcinomata and round-celled solid carcinomata, which may be either simple, scirrhus, or medullary; colloid cancer may occur in the cylinder-celled or round-celled forms.

The macroscopic appearances that carcinomata of the intestines may assume are varied. Frequently the tumor assumes a saucer-like form, having a necrotic ulcerated centre and elevated, indurated edges. Again, it is common to find the tumor extending about the entire lumen of the bowel in a girdle-like manner. Considerably rarer is the cauliflower-like mass of a papillary carcinoma. The tumors vary greatly in size. As the growth is dependent, to a great extent, upon the amount of epithelial tissue present, the larger forms are more commonly found among the medullary and simple carcinomata. The scirrhus forms seldom assume very great dimensions, and on account of their density and small size they rarely undergo very extensive ulceration. They have a particular tendency to encircle the entire lumen of the bowel, and consequently stenosis is one of the most constant results. Colloid cancers, which are relatively most common in the rectum, tend to infiltrate extensive areas of the intestinal wall.

**Obstruction.**—Both the degree and character of the obstruction differ materially in the various types of carcinoma and in individual cases. It may result in one of three ways. The carcinoma may produce an actual stricture of the bowel, as is most commonly seen in annular carcinoma, especially when of the scirrhus form. The same result may occur in the case of an annular carcinoma of a softer variety when in reaction to the carcinoma there is proliferation of the connective tissue of the bowel wall. In the second place, obstruction may result when the carcinoma so infiltrates the bowel wall as to materially increase the thickness of the intestinal wall and thus encroach upon the lumen. This is seen especially in colloid carcinoma, which tends to infiltrate the entire circumference. Lastly, obstruction may result when the



carcinoma growing from the intestinal wall projects so far into the lumen as to occlude it.

**Stagnation of the Intestinal Contents and Dilatation of the Intestine.**—These are conditions which are the direct result of the obstruction offered by the carcinoma. Not infrequently the stagnated contents just above the carcinoma become inspissated and hard, so that in palpating through the abdominal wall this mass may be mistaken for the tumor itself. This error probably accounts for those cases in which a large tumor is diagnosed, but in which one of small size is found on operation or postmortem examination.

Dilatation of the intestine consequent upon carcinomatous obstruction may be either acute or chronic. Chronic dilatation results in those cases of slowly progressive obstruction in which the bowel above the point of obstruction has time to accommodate itself in part to the obstruction. Acute dilatation may result in those rare cases in which the obstruction is of rapid formation, but is much more commonly found as a terminal phenomenon in chronic dilatation. Hypertrophy of the wall cannot go on indefinitely, and there naturally occurs a time when the pressure resulting from the force of the peristalsis above and the obstruction below overcomes the resistance of the bowel wall and it balloons out. Occasionally in carcinoma of the colon acute dilatation of the cecum is found, although the portion of the colon above the obstruction is not dilated. The explanation of this peculiar phenomenon probably lies in the fact that the cecum is subjected to the combined pressure of the peristalsis of the small intestines and the reverse peristalsis of the portion of the colon between the obstruction and the cecum. Rupture of the intestines in acute dilatation may occur.

**Adhesions.**—In the majority of cases of carcinoma of the intestine of some duration, adhesions are found between the peritoneal covering of the area involved and some other portion of the peritoneum. They may bind the intestines to the abdominal wall, or coils of intestines to each other or to any of the abdominal or pelvic viscera with which they come in contact. Frequently the adhesions are not limited to the region of the cancer but involve areas for some distance surrounding it, and at times the adhesive process produces a fusing or matting together of the entire abdominal and pelvic contents.

**Perforation.**—Perforation into the general peritoneal cavity may occur when the destructive processes are so rapid as to prevent the formation of adhesions. More common is perforation into a walled-off sac of the peritoneum or into one of the hollow abdominal or pelvic viscera. In this case there is always first a binding down of the carcinomatous intestine to the portion concerned, and subsequently a perforation. The rupture and the resulting fistula may be between two portions of the intestines, or between the intestine and the stomach, bladder, or uterus. Even perforation of the abdominal wall may occur.

**Peritonitis.**—A generalized peritonitis may result when perforation occurs into the general peritoneal cavity, or a localized peritoneal abscess forms when perforation occurs into a walled-off portion of the peritoneum. Peritonitis, either general or localized, may occur when there

is no actual perforation, in all probability from increased permeability of the degenerated carcinomatous wall.

**Metastasis.**—The commonest seats of the metastases from intestinal carcinoma are the lymph nodes, liver, and peritoneum. There is some difference of opinion as to the frequency of metastasis, especially from the large intestine. Müller, Hausmann, Maydl, and Rupp claim that metastasis to the lymph glands occurs late in carcinoma of the large intestines, and especially the rectum, while Hauser and others have found it early.

**Symptoms.**—As carcinoma in the different portions of the intestinal tract gives rise to essentially different groups of symptoms, the clinical features will be dealt with according to the location of the growth.

**Carcinoma of the Duodenum.**—The average age at which carcinoma of the duodenum occurs, according to the statistics of Rolleston based on 53 cases, is 51.6 years. It is rather more frequent in males than in females. Of 54 cases, 41 were males.

Carcinomata of the duodenum can be classified, according to their location, into those of the first or superior horizontal portion, those of the second or descending portion, and those of the third or inferior horizontal portion. Moreover, the symptoms usually differ materially according as the tumor is located in one or another of these portions. These differences are dependent primarily upon the seat of the tumor in its relation to the papilla of Vater, which is situated in the descending portion. On account of this relationship between the seat of the tumor and the symptomatology, Boas has proposed the use of the term suprapapillary, circumpapillary, and infrapapillary carcinoma.

*Suprapapillary carcinoma* presents in a general way the symptoms of carcinoma of the pylorus, especially those that are due to the purely mechanical effects of the latter. There is dilatation of the stomach with vomiting of the stagnated contents. At times the vomitus contains blood. Since the gastric mucous membrane is not involved in the carcinoma, free hydrochloric acid is usually present and consequently lactic acid and other products of fermentation are not present as in carcinoma of the pylorus. According to the Fenwicks, a tumor is palpable in 60 per cent. of the cases. When palpable it is found to be less movable than carcinoma of the pylorus and is situated more to the right. Despite these points the diagnosis is frequently an impossible one.

*Circumpapillary carcinoma*, or carcinoma of the second portion of the duodenum, may present somewhat different symptoms depending upon whether the growth involves the papilla or not. If it does not the symptoms are either those of carcinoma above or below the papilla. When, however, as is usually the case, the papilla is involved, more characteristic symptoms present themselves. The symptoms of pyloric obstruction may be present, but in addition there are the symptoms of obstructive jaundice. The stools are clay-colored, the tissues and urine deeply bile-stained, the liver enlarged, usually tender, and digestive and other disturbances dependent upon the obstruction to the flow of the bile and pancreatic juice present themselves. These symptoms are not constant, for with the occurrence of ulceration the obstruction may

be partially relieved and the escape of bile made possible. Subsequently the obstructive symptoms again present themselves, perhaps to be followed by another intermission. The ulceration gives access to an ascending infection of the biliary channels, so that a suppurative cholangitis may supervene, as indicated by an increase in the size and tenderness of the liver, chills, fever, and leukocytosis.

The severity of the gastric symptoms is dependent upon the degree of the stenosis caused by the cancer. If the growth should extend toward the pylorus, and at the same time ulceration in the neighborhood of the papilla occur, the symptoms of suprapapillary carcinoma would supervene. Similarly, if the growth extended toward the third portion of the duodenum, and ulceration about the papilla occurred, the symptoms of infrapapillary carcinoma would present themselves. In many of the cancers in this location, and especially in those in which obstructive jaundice is the predominant feature, the differentiation from carcinoma of the ampulla of Vater or of the lower end of the common duct or of the head of the pancreas is extremely difficult. The occurrence of intermissions in the jaundice and the development of a suppurative cholangitis speak strongly for circumpapillary carcinoma. When a tumor is palpable it is felt as an immovable, hard mass deep in the right hypochondriac region near the midline. Either diarrhoea or constipation may be present and anemia and cachexia supervene.

*Infrapapillary carcinoma* characterizes itself by the symptoms of gastric obstruction associated with the vomiting of bile and pancreatic juice. The regurgitation of these fluids into the stomach neutralizes the acidity of its secretion, so that, although no free acid is found, the combined acidity may not be greatly decreased. The presence of the pancreatic secretion may be determined by its lyptic action as well as its proteolytic action in alkaline media. The tumor is at times palpable as a firm, immovable mass near the midline.

**Carcinoma of the Ileum and Jejunum.**—Carcinoma of the ileum and jejunum presents symptoms for the most part similar to those of the first portion of the colon. There is constipation or alternating constipation and diarrhoea. More or less definite symptoms of obstruction may present themselves, but these are not so frequent or marked as in cancer of the colon, on account of the more fluid contents of the bowel in the small intestine. Pain is one of the most constant symptoms, and it is frequently of a colicky character. It is less definitely localized than is the pain of carcinoma of the large bowel. Occult blood is almost always present in the stools, and at times visible blood appears. Occasionally large hemorrhages occur. Although in some cases the tumor can be felt, this is by no means constant. When it can be felt it is characterized by its great movability unless it has been bound down by adhesions. On account of this, it is extremely prone to prolapse and is consequently not infrequently found in the lower abdomen or the pelvis. Cachexia and anemia sooner or later make their appearance. As a rule, these symptoms are more marked than in carcinoma of the large intestine, for, other things being equal, the nearer a carcinoma is to the stomach the more profound are the cachexia and anemia.



**Carcinoma of the Colon.**—Pain is a frequent but not invariable symptom. Some cases run almost the entire course, even to the development of a palpable tumor and marked cachexia, without the occurrence of pain. The majority of cases, however, manifest some degree of pain. It may vary from a vague sense of discomfort to a symptom of great severity, but seldom reaches the extreme until obstruction becomes marked or absolute. Early in the course the patient occasionally complains of diffuse abdominal pain without definite localization. Frequently accompanying this is a sense of pressure or dragging in the abdomen. Later the pain becomes more localized. Occasionally the pain is referred to distant parts, so that a patient with carcinoma of the cecum may complain of pain in the left iliac fossa, or *vice versa*. This is a fact that should constantly be borne in mind in order to avoid errors in localization in case operation be undertaken. Another confusing phenomenon is referred pain along the course of the anterior crural or sciatic nerves and due to pressure on the intra-abdominal plexuses.

The variety of pain that is of greatest significance in the diagnosis of carcinoma of the intestine is colic. The attacks of colic are due to the progressive stenosis and the consequent distension and tonic peristaltic activity of the intestines above the stenosis. Not infrequently these paroxysms constitute the first symptom of which the patient complains. Generally the pain is diffuse throughout the abdomen, although occasionally the patient describes it as more or less localized. At times a cathartic brings on the first paroxysm of colic. The pain may be felt by the patient to move from one position to another until it comes to an abrupt termination with a violent cramp, indicating the location of the obstructive growth.

A feature that practically always accompanies these attacks of colic is constipation. It is one of the most constant and frequently one of the earliest symptoms of intestinal carcinoma, and its occurrence in an individual past middle life should always excite one's suspicion. It is progressive in character, but it is occasionally interrupted by periods of normal activity of the bowels. These interruptions are sometimes due to ulceration of the tumor reestablishing the lumen that had previously been stenosed, and consequently such periods may be accompanied by the appearance of blood, mucus, and pus in the stools. Relief of constipation may, however, be due also to a more fluid condition of the intestinal contents at certain times. Again, periods of diarrhoea are by no means infrequent in the course of intestinal cancer.

**Tumor.**—A palpable tumor is the most reliable and most important symptom. Its detection is not, however, essential to the diagnosis. Some cases run their entire course without the development of a palpable tumor at any time. In the majority of cases careful and repeated examinations reveal a mass. The tumor may vary in size from that of a large nut to that of a child's head. In consistency it contrasts markedly with the surrounding abdominal contents, frequently feeling as firm as cartilage. It is round or irregular in form and its surface may be smooth or nodular. The infiltrating tumors, when they involve extensive areas of the bowel, give the impression to the palpating hand of a thick, solid

cord. When a tumor is very small, percussion over it elicits a note not differing from that of the surrounding intestines. The larger tumors are usually dull to percussion. Pressure usually causes more or less tenderness, which is proportionate to the degree of spontaneous pain. The movability of carcinoma of the large intestine, unless it be bound down by adhesions, is one of its most characteristic features. This is especially true of carcinoma of the transverse colon and the sigmoid, but almost equally so of carcinoma of other portions of the large bowel.

A condition intimately associated with the tumor of intestinal carcinoma, and prone to cause confusion with it, is the tendency to fecal impaction above the point of obstruction. It is not unusual for this mass to become so inspissated and compact as to cause the greatest difficulty in differentiating it from the carcinoma and lead to great misconceptions of the size of the growth. Usually, however, the consistency of this fecal mass is more doughy than that of the carcinoma, and unless the stenosis be complete, laxatives and enemata may clear up the question. Other phenomena that can at times be clearly observed are active peristalsis and distension of the portions of the bowel just above the carcinoma. They are both dependent upon the degree of the stenosis. In patients with thin abdominal walls, in whom hypertrophy of the intestines has occurred above the stenosed area, active peristaltic waves are frequently visible and at times serve as a means of localizing the growth. In carcinoma of the cecum the peristalsis of the small intestine is seen in the central and lower portions of the abdomen, while in carcinoma of the lower portion of the colon these movements are seen in the course of the large bowel.

Gaseous distension, as a result of the stagnation of the intestinal contents, is at times so general that the portion involved cannot be determined by physical examination. In other cases, however, this distension is limited to the segment immediately above the carcinoma, and its observation is then of considerable value in the determination of the seat of the growth. If the distension is found to extend as far as the sigmoid, this would point to the latter portion being the seat of the involvement, whereas if only the transverse and ascending portions of the colon are distended, the localization would in all probability be at the splenic flexure. In carcinoma of the hepatic flexure the ascending colon would be the natural seat of the distension.

The feces occasionally furnish valuable information of the possible existence of a carcinoma of the large bowel. The form of the feces is dependent upon the degree of the stenosis affected by the carcinoma. When the carcinoma is low down and the stenosis is of high degree, the feces are generally of small diameter and either circular or ribbon-shaped, or rudely rectangular in cross-section. Blood, pus, and mucus, either macroscopically or microscopically visible, are not of themselves diagnostic of carcinoma, but are indicative of an ulcerative process in the intestines. Blood and pus are derived from the ulcerated area itself, while the mucus is a product of the catarrhal inflammation of the neighboring mucous membrane. Blood may be present even when ulceration has not occurred. In such cases it proceeds from small

erosions of the mucous membrane, sometimes the result of the mechanical irritation of the fecal masses. Pus is always an indication that ulceration has occurred. The association of pus and blood is of considerable diagnostic significance, for they occur together only in the most severe forms of intestinal ulceration. Shreds of tissue with the histological features of carcinoma may be present, and are of the greatest diagnostic significance. They are, of course, present only when ulceration has occurred.

Cachexia and anemia are constant features of the later stages and do not differ from the cachexia and anemia of carcinoma in general, but are usually of later development in carcinoma of the large intestine than in carcinoma of the small intestine or stomach.

**Complications.**—Acute intestinal obstruction may occur at any time from kinking by bands in the neighborhood of the carcinoma, or volvulus or intussusception induced by the growth, or from the impaction of a foreign body in the partially stenosed lumen, or the simple paralysis of the bowel above the stenosis. Peritonitis may result from rupture or from direct extension through the ulcerated intestinal wall. A localized peritoneal abscess may occur when adhesions have formed around the site of the peritonitis. Perforation of a carcinoma of the large intestine into another hollow abdominal viscus occasionally occurs. Perforation of a carcinoma of the transverse colon into the stomach forming a gastrocolic fistula can be recognized by the presence of fecal vomiting and diarrhoea in which the stools contain undigested food particles. Perforation into another portion of the intestine may occur, and it is a peculiar fact that perforation of a carcinoma of the large intestine is more prone to occur into another portion of the large intestine than into the small intestine. Perforation into the bladder can usually be recognized by the discharge of fecal elements with the urine.

**Treatment.**—When feasible, surgical treatment is employed, whether it be for removal of the growth or to overcome the results of stenosis. When surgical intervention cannot be resorted to, much can be done for the relief of the patient. The principal object is the prevention of fecal accumulation above the tumor. Of the means to guard against it the most important is the administration of such foods as contain a minimum of waste material, and in such form as to be most easily digested and absorbed. Small doses of laxatives may be frequently administered, and their action may be furthered by the occasional employment of oil enemata.

## SARCOMA AND LYMPHOSARCOMA OF THE INTESTINES

Sarcomatous and lymphosarcomatous involvement of the intestines are much rarer than carcinomatous. Whereas, among the autopsies in the General Hospital of Vienna, from the years 1882 to 1893, 243 carcinomata of the intestines were found, there were but 3 cases of sarcoma of the intestines and 9 cases of lymphosarcoma. In Bern 41 cases of carcinoma of the intestines were found to 1 of sarcoma. In contradistinction to the more frequent involvement of the large intestine as



contrasted with the small intestine by carcinoma, sarcoma and lymphosarcoma involve the small intestine at least equally as frequent as they do the large intestine. Of 32 cases of intestinal sarcoma selected by Krüeger, 16 were of the small intestine and 16 of the large intestine. In the 12 cases of sarcoma and lymphosarcoma occurring in Vienna, 8 involved the small intestine and 4 the large intestine.

The various portions of the small intestine are apparently involved with about equal frequency. In a series of cases collected by Libman, 15 were in the duodenum, 18 in the jejunum, and 14 in the ileum. In the large intestine the rectum is most frequently involved, and next in frequency the ileocecal region. Jopson and White collected 22 cases of sarcoma and lymphosarcoma involving the large intestine.

Lymphosarcoma apparently takes its origin from the lymphatic tissue of the intestinal wall and has a great tendency to involve extensive areas of the wall by a process of infiltration. Sarcomata arise from the connective tissue of the submucous layer of the intestinal wall. Histologically, the most frequent form is the small round-celled sarcoma, but large round-celled, spindle-celled, and mixed forms may occur. These tumors also have a marked tendency to infiltrate extensive areas of the bowel wall, but at times they are more globular in form, when they may attain the size of a child's head. When they attain the latter proportions they frequently undergo central softening. They may occur at any age but are most frequent under forty years of age. They are commoner in males than in females.

**Symptoms.**—The symptoms of sarcoma of the intestines differ materially from those of carcinoma. In sarcoma the local symptoms remain in the background, and usually attract attention long after the constitutional effect is noticed. This is due primarily to the fact that there is not the tendency to stenosis of the bowel in sarcoma and lymphosarcoma that is present in carcinoma. Sarcoma and lymphosarcoma invade the intestinal wall and tend to extend longitudinally along the bowel or into the muscular coat, causing weakening and consequent dilatation of the bowel; in consequence of these modes of extension there is little tendency to intestinal stenosis. Consequently, in the majority of cases there is marked wasting and anemia before the symptoms point to any extent to the intestines. In a minority of cases the symptoms of obstruction may occur as a result of the growth of the tumor toward the intestinal lumen, or the destruction of the muscular elements of the wall may lead to paresis and consequent obstruction. Pain and diarrhœa are occasional symptoms. Blood, either occult or visible, may be found in the feces, but aside from this the examination of the stools reveals no characteristic features. Occasionally fever as high as 101° and 102° is an accompaniment of sarcoma or lymphosarcoma of the intestines. Local examination will, in the majority of cases, reveal a tumor. Generally, this is in the nature of greatly thickened coils of intestines, but occasionally it is of a more circumscribed nature. Metastasis to the mesenteric lymphatic nodes may occasion greatly increased tumor masses. The duration contrasts with that of carcinoma of the intestines;

in the majority of cases the patient dies in from four to eight months after the onset of symptoms.

**Treatment.**—Excision of the growth offers the only possibility of cure. Medical treatment can be directed only to the alleviation of symptoms.

### BENIGN TUMORS OF THE INTESTINES

Benign tumors of the intestines are of rare occurrence. In many cases they present no symptoms whatever, the first indication of their presence being their observation at autopsy. In other cases they give rise to various symptoms, but these are seldom characteristic.

**Adenoma.**—These are the most frequent benign neoplasms of the intestines. The tumors take their origin from the glands of Brunner and Lieberkühn, and are usually either polypoid or papillomatous, more frequently the former. Their size varies from that of a pea to that of an orange; they are firm or soft but usually vascular, and bleed on handling. They are usually multiple. Luschka has reported a case in which he counted over a thousand tumors. This condition of multiple intestinal adenomas is termed by Hauser “polyposis intestinalis adenomatosa.” The tumors may be diffusely distributed, but are usually most numerous in the colon and rectum. In children they tend to prolapse, and thus may become gangrenous or give rise to serious hemorrhages. Not infrequently polypoid adenomas give rise to carcinomas; Quénu and Landal found carcinoma in 20 cases of 42 they studied. Multiple polypoid adenomas are most frequent in children from four to seven years of age. In 4 of the 13 cases reported by Post the condition appeared to be hereditary, and Niewack has reported cases showing a family predisposition.

**Lipoma.**—These may be broad-based or pedunculated, and submucous or subserous; they may be small or as large as a child's head. When they assume the latter proportions they frequently produce obstruction; somewhat smaller growths may induce intussusception. They are found somewhat more frequently in the large than in the small intestine. Of 36 cases collected by Dewis, 19 were in the large intestine. The subserous lipoma frequently develops from the epiploic appendages. When pedunculated, the pedicle may atrophy and the growth may lie free in the peritoneal cavity. A submucous lipoma may become detached and be expelled by the rectum.

**Myoma.**—Myoma of the intestines is rare. It occurs oftener in the small than in the large intestine and may be internal or external. The former probably takes its origin from the muscularis mucosa, the latter from the external muscular coat of the intestines. Steiner, in his exhaustive analysis of benign tumors of the intestines, reported 19 cases of internal and 15 of external myoma. They are more commonly found in the ileum and jejunum than in the duodenum and large intestine. These tumors may have a broad, flat base and appear more as localized thickenings of the intestinal wall, or they may be pedunculated, thus taking the form of a polyp. Occasionally there is an extensive distribution of fibrous tissue with the muscular tissue (fibromyoma).

**Hemangioma and Lymphangioma.**—Hemangioma and lymphangioma are rare. McCallum collected 6 cases of hemangioma of the small intestine. They are usually cavernous as distinguished from telangiectatic hemangiomas; as a rule, they are small, flat, and multiple.

**Symptoms.**—Benign tumors of the intestines may not give any indication of their presence or they may present symptoms of a more or less definite character, and at times give rise to conditions of great severity. In multiple intestinal polyposis, hemorrhage and diarrhoea are the most frequent symptoms. If the lesions are located in the colon and rectum, tenesmus may be associated. The stools frequently contain large quantities of mucus. A rectal examination should never be neglected, as not infrequently the diagnosis will be made by finding numbers of the polyps springing from the wall of the rectum. In these cases the polyps are especially liable to constant irritation, and the presence of blood is a frequent symptom. When these adenomatous polyps undergo carcinomatous degeneration the symptoms of cachexia appear.

In myoma, fibroma, and lipoma, hemorrhage and frequent stools, with mucus, may again be the predominant symptoms, but they occur much less frequently than in the multiple polypoid tumors above described. If the tumor is small and situated above the rectum or sigmoid, it usually remains undiscovered. If it is of larger size it may produce a slowly progressive obstruction, or, by inducing intussusception, cause acute obstruction. Steiner records 7 instances of intussusception in 18 cases of large intestinal myoma. When the tumor is of considerable size it can frequently be palpated as a firm, nodular, rather freely movable mass. If it is in the lower part of the large intestine and extends downward it may be palpated or seen in the rectum. Angioma may give rise to extensive hemorrhages. It is impossible to make more than a presumptive diagnosis on the basis of intestinal hemorrhages in an individual previously healthy and in whom no other cause for the condition can be determined.

**Treatment.**—The internal treatment of benign tumors of the intestines is limited to the treatment of the various symptoms. When, however, the symptoms are of sufficient severity or when the tumors are situated in the rectum and are consequently of easy access, surgical treatment is warranted. In case the tumor causes obstruction by occlusion of the lumen or by producing intussusception, operation must be undertaken. In case of hemorrhage of alarming severity from angioma or other benign tumor, operation may be employed. In those instances in which benign tumors are found in the rectum, even when they give rise to no symptoms, they should be removed on account of their tendency to undergo malignant change, as well as the possibility of dangerous hemorrhage.

## EMBOLISM AND THROMBOSIS OF THE MESENTERIC ARTERIES

Occlusion of the mesenteric arteries by embolism or thrombosis constitutes a condition of considerable clinical importance. In an analysis of 214 cases published by Jackson, Porter, and Quimby, in 1907, there



were 197 instances in which an accurate study of the anatomical details was obtainable. Among these, 120, or 61 per cent., were cases of arterial obstruction, and 77, or 39 per cent., of venous obstruction. Embolism is considerably more frequent than thrombosis, the former condition having been present in 63 of 83 cases studied by Gallavardin.

**Etiology.**—Endocarditis and atheromatous conditions of the aorta or of the trunks of the mesenteric arteries are the important conditions antedating embolism. *Arterial thrombosis* is liable to occur when there has been severe enteritis or infective conditions of the intestinal tract, as a result of which bacterial invasion into the bloodvessels takes place. Litten claimed that he had found thrombotic occlusion of the arteries as a consequence of diseased conditions of the arterial lining, but the correctness of his observation has been doubted. Syphilitic endarteritis has also been claimed as a cause of thrombosis, as has direct abdominal injury. *Venous thrombosis* may occur as the result of cirrhosis of the liver, thrombosis of the portal vein, and other conditions causing stasis in the portal circulation.

Embolism and thrombosis of the mesenteric vessels occur much more frequently in men than in women. Jackson, Porter, and Quimby found 64 per cent. in men and 36 per cent. in women. Over half their cases were observed between the ages of thirty and sixty years.

**Pathology.**—The superior mesenteric artery is affected much more frequently than the inferior. The occlusion may involve the trunk of the vessel or one of the terminal branches. Sometimes it affects only the small terminals within the intestinal wall itself. In the last-named cases small ulcerations of the mucosa are met with. The results of venous thrombosis are practically indistinguishable from those of arterial occlusion. There may be a single occlusion of the trunk vessel, or multiple obstructions of small branches. In either case changes occur in the mesentery and bowel embraced in the distribution of the obstructed vessel. The mesentery and the bowel become intensely engorged with blood and assume a dark red and soon almost black color. Hemorrhagic extravasations take place into the tissues, and exudations of hemorrhagic fluid into the abdominal cavity and into the lumen of the bowel occur. The whole lesion is practically a hemorrhagic infarction of the affected area. The affected tissues may undergo rapid necrosis or gangrene, and perforative peritonitis may ensue. In the majority of cases a line of demarcation is observed.

The lesions are usually met with in the small intestine, which is supplied by the superior mesenteric artery. In the rare cases in which the inferior mesenteric vessel is involved the lesions are situated in the large bowel. Partial restoration, through the development of a collateral circulation, has been observed in a few instances.

**Symptoms.**—Two groups of cases are distinguishable, an acute and a chronic, the majority of the cases belonging to the former. In these there is sudden abdominal cramp or colicky pain, followed by nausea and vomiting. The vomitus at first consists of the contents of the stomach, but very speedily becomes hemorrhagic. Very soon diarrhoea sets in and also becomes of hemorrhagic character. In other cases

hemorrhage does not occur, and the symptoms are practically those of an acute intestinal obstruction caused by the paralytic condition of the affected portion of the bowel. The patient's temperature usually falls decidedly, he breaks into profuse perspiration, and frequently sinks into more or less profound collapse.

In some cases pain is wanting, and the earliest symptom may be a hemorrhagic diarrhœa. Pain, however, is usually a conspicuous symptom. In some instances the patient may suffer with repeated attacks of colicky pain, extending over a considerable period of time, without characteristic symptoms of vascular occlusion. In the more acute cases, whether of the hemorrhagic type or of the form suggesting acute intestinal obstruction, intense abdominal pain of almost continuous character, or recurring in paroxysms, is met with. In over half the cases the pain is general. In the others it is limited to one or another region of the abdomen. Local tenderness on pressure may develop, and sometimes becomes extreme when peritonitis has set in.

*Hemorrhagic diarrhœa* is the most conspicuous and significant symptom, although it is not always present. The amount of blood sometimes becomes excessive; and usually there is rapid succession of movements each containing a considerable quantity of blood. When the hemorrhage is marked, the blood may be quickly passed and is only slightly altered. In other cases, black, tarry movements and a highly offensive odor indicate a longer retention within the bowel. Distension of the affected area of the bowel sometimes develops rapidly, and general abdominal distension occurs in the cases in which intestinal obstruction is the important consequence of the vascular occlusion. In some instances a palpable tumor has been discovered in the abdomen, the mass being caused by the infiltrated mesentery and bowel.

In the more chronic cases, which include most of the instances of venous thrombosis, as well as some cases of arterial occlusion, the onset may be insidious and the symptoms of a remittent type. At times there are no abdominal symptoms of any sort; or, at most, vague and indefinite manifestations.

The clinical course may be exceedingly rapid. Jackson, Porter, and Quimby found, in their analysis, that 20 per cent. of the cases of either arterial or venous occlusion had a duration of but twenty-four hours; and 18 per cent. and 22 per cent. of the venous and arterial cases, respectively, a duration of but two days. In 8 and 10 per cent., respectively, the duration was three days. Of the prolonged cases, those due to venous closure showed gradual and continuous progression, while the arterial cases were more apt to present interrupted attacks. In the very acute cases, after the initial pain and vomiting, rapid distension of the abdomen, cessation of peristalsis, and speedy death mark the course of the disease.

**Diagnosis.**—The rules laid down by Gerhardt are still followed with advantage: (1) There must be a source of embolism. (2) Copious intestinal hemorrhage unexplained by organic disease of the bowel or by portal obstruction. (3) A rapid and marked fall of the temperature. (4) More or less severe colicky abdominal pains. (5) Distension of

the abdomen and the accumulation of free abdominal fluid. (6) The occurrence of embolism elsewhere, before or simultaneous with obstruction of the mesenteric vessels. (7) The discovery of a palpable mass.

**Prognosis.**—With few exceptions, the disease terminates fatally. In the statistics before quoted there are recorded 14 cases in which the diagnosis seemed reasonably accurate and in which recovery ensued. This favorable termination can occur only when a collateral circulation is speedily established.

**Treatment.**—This is purely surgical. Jackson, Porter, and Quimby refer to 47 cases in which an exploratory laparotomy was undertaken. The mortality in these cases was 92 per cent. Four patients recovered.

### ARTERIOSCLEROTIC INTESTINAL DISTURBANCES

Certain painful conditions of the intestine are occasionally met with in the aged and arteriosclerotic, and are of some importance on account of their simulation of organic or inflammatory disease of the bowel. The onset may be abrupt, like that of acute intestinal disturbance, and pain may be severe. Usually there is constipation; and sometimes this is obstinate. Later, and especially after the use of laxatives, diarrhœa may set in. Localized soreness or tenderness may be discovered, but there is rarely marked rigidity of the muscles. The nature of these conditions is uncertain. In some cases, doubtless, obstructive conditions of the circulation play an important part. In a case under the observation of the writer, after a number of attacks, death occurred from a severe paroxysm with obstinate constipation, which was followed by the development of uremia. At autopsy a partial obstruction of a branch of the superior mesenteric artery was found; and the section of bowel supplied by this was intensely engorged with blood. There was not complete obstruction, and no actual hemorrhagic infarction. Ortnier has referred to cases somewhat resembling this, under the title of Intermittent Angiosclerotic Dyspragia of the Intestines. He suggests the resemblance to intermittent claudication, and refers particularly to the intermittent character of the symptoms.

### MUCOUS COLITIS

**Definition.**—The term mucous colitis is applied to a condition in which the patient suffers with various symptoms of disturbance of the stomach and bowels and with the regular or periodic discharge of masses of mucus or mucomembranous shreds or casts of the bowel. The terms *membranous colitis*, *tubular diarrhœa*, *mucous colic*, and *mucous diarrhœa* have been applied, and sometimes, although with insufficient justification, a distinction has been drawn between these as being different forms of disease. It is possible to distinguish cases in which mucous or membranous diarrhœa occur as an independent affection and those in which it is secondary to some other disease of the bowel, but there is no fundamental difference between the cases in which a discharge of masses of



gelatinous mucus occurs and those in which membranes or casts of the bowel are met with.

**Etiology.**—The disease is most common in the middle period of life—that is, between thirty and fifty years; but it sometimes occurs in children or those below thirty years, and occasionally persists after fifty years. It is more common in women than in men, the proportion probably being 5 or 10 to 1. The disease affects persons of a better station of life more frequently than the poor, and is commonly associated with a nervous temperament or with distinct nervous disease. Not rarely it develops in hysterical or neurasthenic women, particularly if they have suffered with dyspeptic symptoms and constipation. It may follow after other forms of intestinal disease, the secondary variety being a frequent accompaniment of such diseases as enteroptosis, chronic appendicitis, partial intestinal obstruction, dysentery, tumors, and long-standing constipation.

The direct cause probably varies greatly. Nutritional conditions, such as are met with in those of reduced strength and those having nervous diseases, seem to play a predisposing rôle. Some authors regard the condition simply as an intestinal neurosis with excessive mucus formation (*myxoneurosis*). Others have the contrary view that the nervous manifestations are entirely secondary and that the disease itself is essentially an inflammatory condition with excessive tendency to mucus formation. French authors have attempted to establish a connection between mucous colitis and metabolic disorders (arthritism). The evidence of such connection seems rather fanciful. Recently it has been claimed that certain bacteria play a part in the causation, among other organisms being the *Bacillus coli communis*.

**Pathology.**—The characteristic feature is the formation of excessive quantities of mucus. This may occur as masses or balls of gelatinous character, which may be discharged as such or mixed with brownish fecal matter of liquid, semiliquid, or even solid consistency; or, more characteristically, the mucus may attach itself to the wall of the bowel in the form of more or less tenacious and laminated membranes, which may subsequently be discharged as skins, shreds, long tape-like bands, or even casts representing quite accurately a mould of the bowel. Probably the commonest form is that in which the skins or shreds of membrane are discharged in masses or mixed with soft or liquid fecal matter. The shreds or casts are somewhat laminated, and may show depressions corresponding with the openings of the glands of the mucous membrane. Epithelial cells may be found clinging to the outer surface. The mucous membrane itself may present an inflamed appearance, but usually there is surprisingly little evidence of any structural disease of the bowel. Often an atonic dilatation of the colon is observed, but in other cases a firm toxic contraction of the bowel causes a narrowing of the lumen and an apparent thickening of the wall.

**Symptoms.**—These are gastric, intestinal, nervous, and nutritional. Usually the patient complains of some form of indigestion or dyspepsia. The appetite is poor and capricious; and the patient accustoms herself to greater and greater restriction of diet, as the result of attempting to

find a dietary that will not cause discomfort. Distension of the stomach, flatulence, heaviness, or pain after eating, nausea, and other gastric symptoms may occur. Sometimes pronounced manifestations of various forms of nervous dyspepsia are present.

Among the intestinal symptoms, constipation and the discharge of characteristic mucus- or membrane-containing stools are most important. The majority of patients are constipated, and the discharge of mucus or membrane occurs from time to time, attended with painful paroxysms of varying grades of severity. In cases in which large casts or abundant membranous shreds are passed, an attack of abdominal pain of great violence may precede this, suggesting some form of intensely acute inflammatory trouble. After the passage of the mucus or membrane the painful attack ceases, but a rawness or soreness of the bowel and abdomen is left which may persist for some time. In the majority of cases such painful paroxysms are exceptional, and not rarely the passage of the mucus or membrane is accompanied by a relief of symptoms that have previously been in evidence, such as intestinal distension, general abdominal discomfort, depression, low spirits, etc. Occasionally, instead of constipation, the patient suffers with continued looseness of the bowels and the passage of large quantities of mucus mixed with fecal matter. Sometimes when shreds of membrane or casts are passed there may be a certain amount of blood streaking the membranes; and in exceptional instances a considerable quantity of blood may be discharged.

On examination, the abdomen is distended or scaphoid. Preceding attacks, there may be increasing distension of the colon, which later gives place to a contracted or scaphoid condition; but in many instances distension is wanting at all times, and on direct examination the colon is found contracted as a hard tube. It may be possible to palpate the ascending and descending colon and the sigmoid flexure. The transverse colon is less commonly palpable.

The patient may for a long time suffer with gastric and vague intestinal symptoms and constipation, and may become increasingly nervous, before the characteristic symptoms of mucus- or membrane-formation develop. In such cases the mucous colitis is probably secondary.

The *nervous* manifestations are usually striking. It is difficult to determine to what degree these are the result of the condition, rather than the predisposing cause of it. Nearly all patients who suffer with this condition are depressed, gloomy, irritable, and of low vitality. Distinct hypochondriacal tendencies may be marked, and sometimes the patient becomes actually melancholy. Reflex nervous disturbances of various sorts may occur, such as weakness and irregularity of heart action, neuralgias, headaches, attacks of migraine, etc.

The *nutritional* condition corresponds with the state of the gastrointestinal tract and of the nervous system. Most of the patients are thin or emaciated, and many become progressively more so with its persistence. Sometimes, however, typical and progressive mucous colitis may occur in neurasthenic or hysterical subjects, who show no loss of weight at all commensurate with the gastric and intestinal disturbance. The patient presents an appearance of anemia which,

however, is frequently deceptive, since an examination of the blood may reveal a practically normal condition.

**Complications.**—In some cases the passage of *intestinal sand* is observed. This presents itself as a reddish deposit, resembling brick-dust, or as a grayish or white powder, which consists of phosphate and oxalate and carbonate of calcium with magnesium and iron. A small amount may be passed with each movement, or sometimes large quantities may be discharged from time to time.

In some cases intense soreness of the bowels and probably actual ulceration result from the separation of firm, membranous formations. In these cases the passage of the membrane may be preceded by painful paroxysms of great violence, and may be attended with the discharge of small or large quantities of blood. After the attack, local soreness in the left side or general abdominal tenderness may persist.

Various disorders of the pelvic organs occur in women suffering with this disease; among others, endometritis, menstrual irregularities, dysmenorrhœa, and neuralgic affections localized in the pelvic region. Occasionally, membranous dysmenorrhœa and membranous cystitis have been found combined with membranous colitis.

**Diagnosis.**—Examination of the stools alone enables the physician to diagnose the condition. Neglect of such examination may be the cause of regarding cases of mucous colitis as various sorts of primary nervous disease. Secondary mucous or membranous colitis associated with organic diseases of the bowel, such as chronic appendicitis, adhesions, diverticula, and tumors or strictures, may be indistinguishable from the primary variety. Usually, however, the organic conditions named serve to localize the symptoms and indicate the association.

**Prognosis.**—Mucous colitis is essentially a chronic disease, which tends to continue and increase, although it is not often directly fatal. The general health may be so greatly undermined and nervous vitality so impaired that the patient falls a prey to other conditions. A large proportion of cases (perhaps 50 per cent.) eventually improve to such an extent that, although the health of the individual may be permanently impaired, the actual disease no longer manifests itself. In other cases the disease persists with more or less unabated intensity up to the time of death. Under continuous treatment some improvement is usually obtained, but the chronicity of the affection is such that few patients continue the treatment long enough to obtain the full result possible.

**Treatment.**—The general hygiene and the diet are the most important considerations. Outdoor exercise and suitable occupation are essential. The majority of patients suffer from a sedentary life and a lack of suitable occupation. Not rarely, forced exercise may bring about decided relief, particularly in those cases in which general nervous depression has been augmented by lack of occupation. In some cases, active treatment of the gastric digestion may prove helpful. Increasing doses of *nux vomica* with bicarbonate of soda or the use of digestives may be beneficial.

The dietary treatment may follow one of several rather different plans. Certain authors insist upon the necessity of limiting the dietary decidedly so as to exclude all irritating and unabsorbable matters. They,



therefore, exclude vegetables containing large amounts of cellulose and prescribe mainly farinaceous articles with milk, eggs, and a limited amount of meat—all of which should be so prepared as to be rather semi-solid or liquid. They advise in addition a rather careful study of the tolerance of each patient for the different articles of diet allowed. On the contrary, other authors following von Noorden advise a rather coarse dietary containing rye bread, whole wheat bread, vegetables rich in cellulose, raw fruit, etc. The immediate effect of the former plan is undoubtedly more satisfactory in most cases and is better, though in some cases the coarser diet may be eventually the best. Whatever plan is adopted it is advisable to see that the patient has sufficient nourishment.

It is important that the intestinal drainage should be maintained, and when constipation is marked some form of laxative is helpful. In many cases the occasional administration of castor oil relieves the patient for some time, and may have a lasting beneficial effect. In some, the administration of very small doses of castor oil several times daily, in combination with such intestinal antiseptics as salol, betanaphthol, guaiacol carbonate, and calomel in fractional doses, may be beneficial. Now and then it is advisable to administer some form of saline purgative or to use medicinal waters for the same purpose. Paraffin oil in doses of one to two teaspoonfuls three times daily, or of one or two tablespoonfuls at night, often gives excellent results if continued patiently for considerable periods.

When the condition seems to affect the lower bowel, colonic douches with simple saline solution, or with water containing fluid extract of hamamelis, small amounts of quinine or nitrate of silver (1 to 5000), may have a beneficial effect. It is rarely desirable, however, to persist in direct colonic medication or flushing, as too long a continuance of this plan of treatment may cause a return of the symptoms, and even an aggravation of them. Some patients are helped by the gentle injection into the colon of ten or twelve ounces of olive or cotton-seed oil at bedtime, to be retained during the night.

Local treatment of the abdomen is useful in some cases. Abdominal massage given by a skilful manipulator, external or intra-intestinal electricity, and high-frequency currents have sometimes been used with advantage. Recently, Wright and others have treated patients by vaccination with killed cultures of the *Bacillus coli*. This method, however, rests upon no certain foundation.

Surgical measures have been used with advantage. Occasionally the removal of a chronically inflamed and adherent appendix has been followed by remarkable improvement. Some obstinate cases have been treated by attaching the tip of the appendix to an abdominal opening and flushing out the bowel daily, or at stated intervals. In other cases an artificial anus has been made in the right iliac region, and has been used to flush the colon thoroughly. The seriousness of such an operation and its generally objectionable features militate against its frequent employment. It has also been suggested that the ileum be anastomosed with the rectum.

## CHAPTER VII

### DISEASES OF THE LIVER, GALL-BLADDER, AND BILIARY DUCTS

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#### THE LIVER<sup>1</sup>

##### DISORDERS OF FUNCTION

THE liver, the largest glandular organ in the body, is of complex structure and is endowed with a multiplicity of functions. Several of the structural peculiarities are mentioned in connection with the discussion of the histology of cirrhosis, and the structural changes that occur in different diseases are discussed under the respective headings. The disorders of the functions of the liver are less well understood.

Inasmuch as health and disease each consists of a sum of variables that have no well-defined limits, overlap materially, and pass gradually the one into the other, it is not surprising that the ultimate beginnings of disease often escape our observation. As regards the liver specifically, if, as for instance in certain infections, the time of the onset of the infection is apparently quite obvious, in many other diseases, especially those of a more insidious onset and more chronic course, the time of onset cannot be determined, and frequently structural alterations are well advanced before obtrusive symptoms develop. It is difficult to believe, however, that normal liver cells can perform their functions otherwise than normally, and, conversely, abnormal function presupposes structural alterations—macroscopic, microscopic, or physicochemical. In some instances these structural alterations cannot be detected by the means of investigation at our command, but their existence cannot be denied, and we must look upon the sensible evidences of disease, the symptoms, as the manifestations of structural alterations already effected. As a rule, noteworthy symptoms are associated with more or less readily demonstrable structural alterations; but extreme disorder of function is not infrequently associated with apparently normal structure, and advanced structural alterations are not incompatible with long life

<sup>1</sup> The best work on the subject is Rolleston's *Diseases of the Liver, Gall-bladder, and Bile Ducts*, 2d edition, Macmillan & Co., 1912, a record of much personal observation, including a thorough review of the literature, with many statistics and selected case-reports in brief. Another excellent book is Quinke and Hoppe-Seyler's *Die Krankheiten der Leber*, 2 Aufl., Wien u. Leipzig, Hölder, 1912.

and freedom from distress. It is essential to correlate function with structure, and to study diseased processes from the structural, the functional, and the chemical points of view.

The functions of the liver may be said to be: (1) To detoxify poisons that enter the body by way of, or are elaborated within, the gastro-intestinal tract, or are perhaps produced elsewhere; (2) to secrete bile; (3) to warehouse some of the excess of fat taken as food and to release it when the supply from without becomes deficient; (4) to warehouse glycogen derived from the carbohydrates taken as food, or from the non-nitrogenous part of the proteins when the supply of carbohydrates is deficient, and to convert the glycogen into glucose and liberate it as it is required; and (5) to assist in the metabolism of the proteins to the extent, at least, of forming urea from ammonia compounds.

Disorder of the functions of the liver may be primary or secondary (to structural alterations in the liver or to disease elsewhere); and it may be partial, involving perhaps only one function, or it may be total, involving presumably all the functions. The belief in a primary general disorder of function is exemplified in the terms torpid liver, biliousness, bilious headache, lithemia, etc., that have been handed down to us by our forefathers. Present-day opinions tend, perhaps unwisely, to minimize the influence of the liver in these disorders; but this seems an almost inevitable result of the knowledge that phenomena commonly attributed to a supposed torpid liver and the other affections mentioned may result from factors that do not involve the liver primarily, if at all, and that uric acid (lithemia), by no means the important factor in disease it was once thought, is not formed exclusively in the liver. The dyspeptic symptoms of a supposed torpid liver are usually due to a gastro-intestinal catarrh set up by dietetic indiscretions, excessive eating (especially of proteins and carbohydrates), the consumption of too much alcohol, etc.; the spread of this catarrh to the diverticulum of Vater and the common bile duct, or perhaps rarely a toxic descending radicular cholangitis, is answerable for the subicteric tint of the conjunctiva and skin. The liver usually participates only secondarily; perhaps toxins are produced in such amounts that the liver cannot neutralize them and they pass over into the circulation, or they are so virulent that they impair the detoxifying function of the liver cells or set up congestive and other alterations in the liver. In either event the symptoms are gastro-intestinal rather than hepatic in origin, and the liver, responding to excessive demands has often, for a time at least, increased rather than decreased functional activity.

There is, however, another series of cases, such as the passive congestion of chronic cardiac and pulmonary disease, in which there is reason to believe that the functional activity of the liver is reduced. It is usually difficult, if not impossible, in these cases to differentiate the symptoms properly referable to disordered functions of the liver from those really due to the defective circulation in general with consequent congestion of the different organs, notably the intestines and the kidneys, and defective elimination.

In another series of cases, more or less complete functional failure



of the liver ensues. These are cases of severe intoxication or infection, in which widespread destruction or disorganization of the hepatic parenchyma occurs. The striking clinical phenomena, which may develop suddenly although they are sometimes preceded by minor symptoms, are for the most part nervous; they are variously designated hepatargia, acholia, cholemia, hepatic auto-intoxication, etc. Headache is a conspicuous symptom, and is soon followed by mental excitement, delirium (which may be very active or maniacal), muscular twitchings, and convulsions; or mental hebetude progressing to deep coma may ensue. Most of these cases are associated with varying grades of jaundice and other phenomena that will be more fully discussed later. From time to time tests for determining the functional activity of the liver have been advanced, but few have withstood critical investigation.

**The Detoxifying Function.**—Certain substances, highly poisonous when administered hypodermically, are much less harmful or entirely innocuous when administered by the mouth. In some cases, perhaps, this detoxification may be brought about by the gastric and the intestinal secretions; but in many cases the poisons are carried by the portal circulation to the liver, and there, probably by a process of oxidation, deprived of their toxicity. This obtains in the case of substances such as curare, nicotine, etc., and to a less extent in the case of substances such as morphine, strychnine, etc. The liver is believed to exert a similar detoxifying action on the toxins of certain bacteria, such as the typhoid bacillus, etc., and on the products of bacterial putrefaction in the intestine, such as indol and phenol. Doubtless in some cases these poisons are excessive in amount or in virulence, and the liver is unable successfully to cope with them. Disturbances in this protective or detoxifying function of the liver are believed by some observers to be the basis of the eclamptic manifestations of uremia, pregnancy, etc.; but the question still awaits solution. Pick<sup>1</sup> also believes that if this detoxifying function is interfered with by an excess of toxin, disturbances of bile production, glycogen storage and uric acid formation may result and that the likelihood of cholelithiasis may be increased by consequent concentration of bile acids. In favor of the connection between disturbance of liver function and auto-intoxication is the co-incident appearance of gall-stone disease, gout, and glycosuria.

There is no doubt that in disease the detoxifying function of the liver is more or less impaired, but there is no trustworthy method of determining and utilizing this as a diagnostic test clinically. The results of some studies by Hawk,<sup>2</sup> suggest the wisdom of restricting the amount of meat in the diet in autotoxic conditions, since the use of meat appeared to increase the toxic phenomena.

**The Lipogenic Function.**—In health the warehousing of fat in the liver is a function of less importance in man than in some of the lower animals, especially those that have little power to accumulate fat in the muscles and other tissues. In disease, however, the liver may store considerable fat, but only when the amount of stored glycogen becomes

<sup>1</sup> *Wien. med. Wchnschr.*, 1912, lxii, 3145.

<sup>2</sup> *Am. Jour. Physiol.*, Boston, 1908, xxi, 259.

much decreased or disappears. Disturbances of fat metabolism may be attended by extremely serious consequences, notably the condition spoken of as acidosis, due to the presence of the acetone bodies—acetone, diacetic acid, and  $\beta$ -oxybutyric acid. Although formed from the fats of the body in certain conditions when the oxidizing powers are reduced, they are directly related to deficiency of glycogen, which may be the consequence of insufficient intake (as in starvation) or of excessive output (as in diabetes).

**The Urea-forming Function.**—The synthesis of urea from ammonia compounds and the availability of disturbances in this function as a test of hepatic insufficiency have also been much studied. *A priori* it is not unreasonable to suppose that in case the activity of the liver be reduced the amount of urea in the urine should be diminished and that of ammonia increased. This opinion has received some support from the experimental studies, by means of Eck fistulæ on dogs, of Hahn, Massen, Nencki, Pawlow, and Salaskin. In jaundice from obstruction the output of urea is usually not affected, although the percentage of ammonia is increased. In cirrhosis, on the other hand, the urea is diminished and the ammonia is much increased—which lends support to the theory of disturbed urea synthesis; but this theory is more or less discredited by the fact that feeding ammonia salts to cirrhotic subjects is not followed by impairment of the formation of urea. Stadelmann advanced the theory of acidosis, seeking to explain the increased ammonia output on the purely chemical basis of the neutralization of an excess of acid (as is seen in diabetes). The volatile fatty acids have been found increased; sarcolactic acid and diacetic acid have also been found, which, in connection with lessening of the alkalinity of the blood and increase of bases in the urine (Münzer and Soetbeer), tends to confirm the theory of acid intoxication.

**The Glycogenic Function.**—This has been much studied with a view to discovering, if possible, departures from the normal and utilizing these in clinical diagnosis. Stoppage of the flow of bile has been supposed to prevent the storing of glycogen. Glycosuria, as a matter of fact, has been observed in certain disorders of the liver, but as changes in the pancreas may also cause it, the occurrence of glycosuria does not prove that the trouble lies in the liver. The obvious inference has been combated by Naunyn, Kausch, and others. The weight of opinion is that alimentary glycosuria is not a trustworthy test of hepatic insufficiency.<sup>1</sup>

A new impetus to the study of alimentary mellituria was given by Sachs, who found that dehepatized dogs showed a lessened tolerance for levulose, but not for dextrose, galactose, and arabinose. Studying the subject clinically, he found that healthy as well as diabetic subjects have a greater tolerance for levulose than for dextrose, and that the subjects of hepatic disease have a lessened tolerance for a like amount of levulose. Strauss, applying these results in a large series of cases, found that 90 per cent. of hepatic subjects presented levulosuria after the ingestion of a measured amount of levulose. His observations have

<sup>1</sup> Churchman, *Johns Hopkins Hosp. Bull.*, 1912, xxiii, 10.

been confirmed by von Halász<sup>1</sup> and Goodman.<sup>2</sup> Alimentary levulosuria thus has been suggested and utilized as a test of hepatic insufficiency. Although its trustworthiness has been questioned by a few observers, such as Landsberg, the weight of opinion is that it is of distinct value. It is much more satisfactory than alimentary glycosuria. Bauer<sup>3</sup> in 1908 suggested galactose for use in tests of liver function; Reiss and Jehn<sup>4</sup> have studied this test and state that it must be accepted with reserve.

Of the many disorders of the liver, alimentary levulosuria seems to be of special diagnostic significance in cirrhosis. It has not been found in many non-hepatic diseases; pneumonic subjects are said to exhibit both spontaneous as well as alimentary levulosuria, but these are not likely to be confused with the subject of diseases of the liver.

### JAUNDICE

Jaundice is a term applied to staining of the tissues with bile pigments which are present in the blood. It is recognized clinically by a yellowish or yellowish-green discoloration of the skin and visible mucous membranes and by the presence of bile pigments in the urine. It is not a disease *sui generis*, but merely a symptom of a wide variety of disorders. Although it indicates some disturbance in the secretion or excretion of bile, and is, therefore, significant of disease of the liver, it occurs also in disorders in which the liver is not involved primarily.

Jaundice occurs in a variety of circumstances. In many cases it results from an obstruction to the free flow of bile. Often the obstruction is obvious and consists of: (1) An obstruction within the common bile duct or the hepatic duct, such as gall-stones, parasites, foreign bodies, etc.; (2) inflammatory, cicatricial, or neoplastic stenosis of the ducts; (3) compression of the ducts from without by tumors of the pancreas, stomach, intestine, gall-bladder, regional lymph glands, kidney, retro-peritoneum, mesentery, etc., inflammatory adhesions, swollen glands, fecal accumulations, aneurism of the aorta or of the hepatic or mesenteric artery; etc.; or (4) kinking or torsion of the ducts in consequence of gastropexia, hepatic flexure, nephropexia, the pregnant uterus, tumors of the abdominal or pelvic organs, etc. In another series of cases—of disease of the liver unattended by gross obstruction of the extrahepatic biliary ducts—the hindrance to the free flow of bile is none the less demonstrable, if less marked and less obvious at first sight; these comprise cases of localized inflammatory processes (abscesses), tubercles, gummas, hydatid cysts, primary and secondary new-growths within the substance of the liver, etc. Jaundice, however, occurs under other circumstances in which apparently the biliary ducts are patent, as in cirrhosis and other diffuse diseases of the liver; in many infections, such as the different

<sup>1</sup> *Wien. klin. Wchnschr.*, 1908, xxi, 44.

<sup>2</sup> *Jour. Amer. Med. Assoc.*, Chicago, 1909, liii, 2054.

<sup>3</sup> *Deutsch. med. Wchnschr.*, 1908, xxxiv, 1505.

<sup>4</sup> *Deutsch. Arch. f. klin. Med.*, 1912, cviii, 187.



types of so-called infectious jaundice, syphilis, yellow fever, septico-pyemia, malaria, pneumonia, typhoid fever, etc.; in intoxications, such as poisoning with ptomaines, phosphorus, arseniuretted hydrogen, chloroform, mushrooms, toluylendiamin, pyrogallol, snake venom, coal-tar products, etc.; in acute yellow atrophy of the liver; in progressive pernicious anemia and hemoglobinemia, and in disturbances of the circulation, such as passive congestion; in the new-born, etc.

**Types of Jaundice.**—Different classifications of the disorder have been made variously based upon the supposed pathogenesis, the etiology, the clinical features or course, etc. It must be apparent that jaundice can result only from: (1) An obstruction somewhere in the course of the biliary tract in consequence of which the bile becomes absorbed by the lymphatics or the bloodvessels—*jaundice from stasis of bile*; or (2) disturbances in the functions of the liver cells, whereby the bile is diverted from the biliary capillaries to the lymphatics or the blood-channels—*jaundice from parapapadesis of bile*. In the one case the disorder involves the bile after it has been formed and entered the biliary channels; in the other it involves the bile pigments while they are still within the hepatic cells. There is comparatively little discussion regarding the nature of the cases due to obvious obstruction of the extrahepatic or the intrahepatic ducts; these are commonly described as *obstructive* or *mechanical jaundice*. Regarding the cases of so-called non-mechanical or non-obstructive jaundice there are different opinions. A mistaken interpretation of surface phenomena led to a classification into: (1) Hepatogenous jaundice, that in which the liver, including the biliary ducts, was obviously at fault, that is, obstructed; and (2) hematogenous jaundice, that in which no disorder of the liver or the biliary ducts being apparent, the bile pigments were supposed to be formed in the bloodvessels in consequence of the destruction of erythrocytes and the conversion of the thus liberated hemoglobin into bilirubin. The work of Naunyn, Minkowski, Stadelmann, and others, proved that all jaundice is hepatogenous—in the sense that bile pigments are formed only in the liver. Nevertheless, the influence of increased destruction of erythrocytes in providing the material (hemoglobin) from which bile pigments are formed in excess (polychromia) in some cases of jaundice cannot be gainsaid; this has led to the use of the term hemohepatogenous jaundice. Since this form of jaundice is found in toxic, infectious, and other conditions associated with destruction of erythrocytes, it is spoken of as toxic, infectious, or hemolytic.<sup>1</sup>

Inasmuch as the etiological factor in many of the cases of so-called non-obstructive jaundice is unknown, it is quite impossible to differentiate them clinically or otherwise, aside from the severity of the symptoms; but the clinical designations, mild and severe, are often quite inappropriate, since the degree of the jaundice and the severity of the other symptoms frequently bear no relationship whatever the one to the other. There can be little question that many of the cases represent only different stages or grades of the one process. In a simple and usually mild form,

<sup>1</sup> Consult Whipple and Hooper, *Jour. Exp. Med.*, New York, 1913, xvii, 593.

jaundice is an accompaniment or sequel of gastro-intestinal catarrh; the direct cause of the jaundice is an extension of the catarrhal process to the diverticulum of Vater or the common bile duct and consequent obstruction to the flow of bile. Since these cases commonly pursue a benign course, and the few that have come to necropsy have revealed only catarrhal papillitis or cholangitis, the disorder is spoken of as simple or catarrhal jaundice (preferably catarrhal cholangitis). In another series of cases in addition to the jaundice there are phenomena of general infection, such as fever, neuromuscular pains, enlargement of the spleen and liver, gastrointestinal disorders, such as vomiting and diarrhoea, nervous manifestations, such as headache, stupor, etc., often leukocytosis, albuminuria, tube casts, etc.; to these cases the term infectious jaundice (Weil's disease) has been applied.<sup>1</sup> The not uncommon epidemic occurrence of such cases warrants the use of the term epidemic jaundice.

Cockayne<sup>2</sup> states that catarrhal jaundice is the sporadic or endemic form of what he calls epidemic catarrhal jaundice, in the majority of cases. He also believes that in addition to sporadic and epidemic catarrhal jaundice, acute yellow atrophy is usually due to the same cause, a specific organism of unknown nature. In other cases the clinical phenomena are more severe, symptoms attributable to hepatic insufficiency (hepatargia), to poisoning by bile acids (cholemia), or to hepatic auto-intoxication (acidosis), supervene, and a fatal issue usually ensues; the condition is spoken of as grave jaundice (icterus gravis). When, in addition, considerable destruction of the liver cells occurs, the term acute yellow atrophy of the liver is employed. No sharp line can be drawn between the cases; mild in the beginning (seemingly catarrhal jaundice), they may progress to the most severe and fatal form (acute yellow atrophy); the degree of jaundice bears no constant relationship to the demonstrable changes in the liver, nor, as already stated, to the severity of the other clinical phenomena; in some cases of unusual and widespread destruction of the hepatic parenchyma the jaundice may be slight, rarely even entirely absent, so that, until such time as the etiological factors shall have been better elucidated, we perhaps must rest content with the terms toxic, infectious, hemolytic, or hemohepatogenous jaundice, as seems best suited to specific cases. Some of the cases are unquestionably examples of typhoid infection of the biliary tract; others are likely due to infection with *Bacillus coli communis*, *Bacillus proteus*, etc.; perhaps others are due to infection by unidentified (anaërobic?) bacteria which, settling in the duodenum, multiply and produce an ascending cholangitis and ultimately more or less destruction of the hepatic cells. Other cases, toxic in nature, result from the poisons transported to the liver by way of the portal circulation. In still other cases the primary action of the poison is on the erythrocytes (hemolysis), in consequence of which an increased amount of free hemoglobin is carried to the liver cells and transformed into bile pigments.

<sup>1</sup> Consult Boggs in vol. i, page 1014 of this work.

<sup>2</sup> *Quart. Jour. Med.*, Oxford, 1912, vi, 1.

**Pathogenesis of Jaundice.**—The mechanism of jaundice due to gross obstruction of the extrahepatic biliary ducts, or to none the less real if less marked obstruction of the larger intrahepatic ducts, is readily comprehended. On the one hand, the outflow of bile into the duodenum is hindered; on the other hand the hepatic cells, even after the common bile duct has been completely occluded, continue to secrete bile (although perhaps in lessened amount than normally), to convert into bile pigments the free hemoglobin brought thither. In consequence, then, of obstructed outflow and of continued production, bile accumulates within the biliary tract, the pressure increases, and the biliary ducts become dilated. It has been demonstrated by Eppinger<sup>1</sup> that this dilatation involves not only the larger biliary ducts but extends to the finest biliary capillaries, which become enormously distended, especially at the points of communication of the capillaries of adjacent rows of liver cells. Furthermore, evidences of the increased pressure are seen in the intercellular biliary capillaries, which become lengthened in the direction of their distal end, dilate ampulla-like, and gradually approach and finally rupture into the lymph spaces between the hepatic cells and the bloodvessels; thence, by way of the thoracic duct, the biliary constituents reach the bloodvessels. That the pathway of the bile to the bloodvessels is by way of the lymphatics and the thoracic duct has been repeatedly demonstrated.

The mechanism of jaundice not due to obvious or gross obstruction of the biliary ducts is not so well understood; it has been variously explained. Frerichs believed that the bile found its way directly into the bloodvessels in consequence of changes in the tension of the contents of the hepatic cells and of the bloodvessels—either an increase in the intercellular pressure or a decrease in the portal pressure. Leibermeister believed that the disordered liver cells lost their ability to retain or fix the bile, and that in consequence it became diffused into the bloodvessels or lymphatics—so-called diffusion or akathektic jaundice. Minkowski assumed a disturbance in the normal currents within the liver cells, so that the bile became diverted from the biliary capillaries to the bloodvessels or lymphatics—jaundice from parapadesis (paracholia of Pick). It is not unlikely that the toxic and infectious causes of this form of jaundice seriously compromise the functional integrity of the liver cells; but it has also been demonstrated that they provoke a radicular cholangitis which obstructs the free flow of bile. Eppinger states that in these cases thrombi made up of coagulated bile occur in and obstruct the biliary capillaries; in consequence thereof, mechanical stasis of the bile develops in the finest biliary capillaries, and, as in cases of gross obstruction of the larger extrahepatic ducts, the biliary canaliculi dilate and ultimately rupture into the pericellular lymph spaces. The bile thrombi are interpreted as a manifestation of biliary inspissation, perhaps related to coagulation of a pathological albuminous exudate (to which the liver cells become pervious); but the basic cause is believed to be marked erythrocytolysis in consequence of which the liver is forced to the production of increased bile pigments. Experimentally,

<sup>1</sup> *Ergebnisse der inneren Medizin und Kinderheilkunde*, 1908, i, 107 (literature).



it has been found that in these cases there is at first an increased formation and excretion of bile (polycholia) and of bile pigments (polychromia); soon, however, the excretion of bile lessens, the bile that is excreted becomes viscid, and finally excretion may cease, which may be attributed to a radicular cholangitis or the biliary thrombi, or both. Thus, although this form of jaundice is properly called toxic, infectious, or hemolytic, it is at the same time hepatogenous and obstructive. The degree of jaundice is determined by the degree and extent of the obstruction rather than by the amount of hemolysis: a high grade of jaundice may occur with comparatively little hemolysis, whereas considerable hemolysis may be attended with only slight jaundice.

*Icterus neonatorum* is a peculiar form of jaundice that develops in from two-thirds to three-fourths of new-born infants on the second or third day of life, and usually fades within a week or ten days. The cutaneous discoloration is slight, and is commonly unattended by other symptoms. The urine is often of normal color, and usually does not contain soluble bile pigments, but may reveal biliary granules or crystals in desquamated renal epithelium. The nature of this form of jaundice is not well understood. It has been attributed to compression of the biliary capillaries by distended portal radicles; to catarrhal cholangitis (Virchow); and to biliary stasis in consequence of the diminutive size of the bile ducts and consequent obstruction (Kehrer and Cohnheim). Frank attributed it to absorption of bilirubin from the meconium; and Quincke has suggested that this bilirubin, which is not converted into urobilin on account of the absence of intestinal fermentation in the new-born, being absorbed, reaches the general circulation by way of the ductus venosus without traversing the liver. Stumpf<sup>1</sup> comes to the conclusion that it does not depend upon an infection spreading from the umbilical cord. Perhaps the disorder is really due to the erythrocytolysis of the early days of life. If this be the true explanation, the pathogenesis is that of hemolytic jaundice. This benign form of jaundice must be distinguished from a more severe and often fatal form that may also occur in the early days of life in consequence of congenital syphilis, septicopyemia, congenital obliteration of the bile ducts, etc.

*Chronic splenomegalic hemolytic jaundice*<sup>2</sup> is a type which has recently received a good deal of attention and which has been described under many synonyms calling attention to its hereditary or familial character, though some cases seem to be purely of an acquired form. In the true familial type the jaundice, which is not very marked, dates usually from birth, or is noticed first during adolescence and occurs in several members of a family, often through a number of generations. The jaundice persists throughout the life of the patient but causes practically no symptoms. As Chauffard has expressed it, these patients are rather jaundiced than sick. The urine and stools are highly colored, the urine containing urobilin, and there is no evidence of biliary obstruction, the

<sup>1</sup> *Wien. klin. Rundschau*, 1910, xlv, 687 (literature).

<sup>2</sup> Consult Chauffard. *Semaine méd.*, 1907, xxvii, 25; 1908, xxviii, 48; Tileston and Griffin, *Am. Jour. Med. Sci.*, Phila., 1910, cxxxix, 847; Thayer and Morris, *Johns Hopkins Hosp. Bull.*, 1911, xxii, 85.

jaundice apparently being due to an excess of biliary pigment resulting from the destruction of the red-blood corpuscles. Chauffard has pointed out that the red-blood cells show an increased fragility when they are exposed to hypotonic solutions of sodium chloride according to the method of Vaques and Ribierre. The spleen is almost invariably enlarged, at times to enormous size, though the liver is usually not enlarged, or only slightly so. These patients have "bilious attacks" quite commonly, even after slight indiscretions in diet; they are apt to have gall-stones (in 5 out of 8 cases coming to autopsy) and pain in the region of the gall-bladder is common. There is moderate anemia.

In the so-called *acquired form* there is not the same clean-cut disease picture; the patients usually show a more intense anemia and the fragility of the red-blood cells so characteristic of the familial cases is wanting. Recovery may occur after prolonged administration of iron in the acquired forms, but apparently cannot be expected in the hereditary cases. Chauffard<sup>1</sup> has lately changed his views on the apparent absence of danger in the congenital cases and states that serious complications may arise, such as cholangitis and cholelithiasis. Splenectomy, which has been suggested, he feels should only be resorted to after thoroughly explaining to the patient the danger of the operation. As Rolleston puts it these patients should live a protected life.

**Effects of Jaundice.**—The clinical phenomena attendant upon jaundice are due largely to the underlying causes of which the jaundice itself is merely a symptom. The symptoms, however, inasmuch as they are related directly to the jaundice and not to the underlying cause, are due on the one hand to the presence of biliary derivatives in the circulating blood, and, on the other hand, to the absence of bile from the intestine. All of the tissues and organs, with the exception of the nervous, are stained with biliary pigments; and in some severe cases of toxic or infectious jaundice the nervous system also may be stained. The staining is due, in part, to the deposition of biliary pigments in the tissues, in part to the circulation of blood and lymph containing undeposited pigments; it is most marked in the skin, mucous membranes, serous membranes, the liver, kidneys, heart, transudates, exudates, etc.

*The Mucous Membranes and the Skin.*—Jaundice is manifested first by a yellowish discoloration of the conjunctivæ; in mild cases the discoloration is demonstrable there only. In the other visible mucous membranes, except that of the hard palate, the jaundice, unless of high grade, becomes apparent only after the tissues, by pressure, have been deprived of blood; the mucosa of the hard palate, however, being normally pale may reveal the discoloration without this.

The skin becomes of a characteristic lemon-yellow, orange-yellow, greenish-yellow, olive, or olive-bronze color. The discoloration is light in many cases of toxic or hemolytic jaundice, in which it is rarely more than moderate in grade; it is light also in mild cases of catarrhal cholangitis; it is darkest in cases of permanent and complete obstruction of the common bile duct, and it may become so dark—olive bronze or

<sup>1</sup> *Bull. méd., Par.*, 1912, xxvi, 1159.

greenish black—as to warrant the designation black jaundice (melanicterus, icterus melas). The intensity of the jaundice in these cases is proportionate to the completeness of the obstruction of the common duct, or, in case the obstruction involve one of the larger intrahepatic ducts, to the size of the duct implicated. The jaundice occurs earliest (sometimes within several hours) in cases of obstruction to the finer biliary ducts and capillaries, on account of the seat of the obstruction; it is delayed, commonly four or five days, in obstruction of the common duct, because the bile accumulating gradually distends the larger ducts and the gall-bladder. Time is required to produce sufficient pressure in the biliary canaliculi to cause their rupture into the adjacent lymphatic spaces and consequent absorption of bile. The pigment for the most part is deposited in the cells of the rete Malpighii, where in great measure it persists, often causing an obvious discoloration until the cells have been desquamated. It is for this reason that the cutaneous discoloration commonly persists a week, perhaps several weeks, after bile pigments have disappeared from the urine.

Of other cutaneous manifestations, pruritus is the most common and distressing. Rarely it precedes the discoloration of the skin; it is likely to develop in cases of jaundice of sudden onset; as a rule it is most marked in protracted and severe cases; but it bears no definite relationship to the duration or the severity of the jaundice. Urticaria, perhaps due to a toxemia, is not uncommon. Considerable sweating, often localized to the palms, etc., is sometimes observed. Local infections, such as boils, occasionally occur. In chronic cases, local telangiectases of the skin (sometimes also of the oral and other mucous membranes) tend to develop, and flat or nodular yellowish, chamois-leather-colored patches (xanthelasma, xanthoma, vitiligoidea<sup>1</sup>) may appear on the skin or mucous membranes. These are most common in the skin of the eyelids, and in the folds and creases of the joints; they tend to be symmetrical in distribution; they have been observed on the gums, in the mucosa of the biliary ducts (perhaps in part answerable for the jaundice), etc. They are believed to be inflammatory or endothelial in origin, and to be due to the jaundice or an associated toxemia.

*The Blood.*—Bile pigments are present in excess in the circulating blood, but whether they exert any deleterious effect on the blood itself has not been satisfactorily determined. The major toxic action of the bile is due to the bile acids—salts of glycocholic and taurocholic acids. Chauffard<sup>2</sup> calls attention to variations in the symptoms depending upon the predominance of one or other of the three component elements of the bile (bilirubin, the bile acid salts of glycocholic and taurocholic acids, and cholesterin). Glycocoll and taurin result from hydrolysis of protein; the source of cholic acid is not definitely known. At the inception of jaundice these acid salts may be found in the circulating blood, but after jaundice is well established they usually disappear from the blood, being apparently produced in lessened amount, although the bile pigments continue to be produced in normal or almost normal amount.

<sup>1</sup> Consult Fitcher, *Amer. Jour. Med. Sci.*, Phila., 1905, cxxx, 939.

<sup>2</sup> *Presse méd.*, Par., 1913, xxi, 81.



In ordinary obstructive jaundice the amount of bile acids in the blood is not sufficient to produce any noteworthy hemolysis; indeed, polycythemia is not uncommon. Pearce, Austin, and Musser<sup>1</sup> have shown that if a splenectomized animal is injected with hemolytic serum jaundice does not occur; they believe that this is due in some way to the anemia which follows splenectomy. Indeed, jaundice is not readily produced in animals with low counts even if the spleen has not been removed. In toxic or infectious jaundice, however, hemolysis is common; usually it is itself the direct cause of the jaundice, but it may be increased by circulating bile acids. Chauffard<sup>2</sup> believes in the possibility of differentiating hemolytic from ordinary obstructive jaundice by the fragility, granular appearance, and small size of the erythrocytes (those from 3 to 6 $\mu$  in diameter increasing to 15 to 18 per cent. of the total number); in obstructive jaundice the erythrocytes are said to be normally resistant, of normal size, and free from granulations. The *coagulation time* of the blood is much increased in jaundice—from the normal three to four minutes to ten to twelve minutes, a fact of much importance when surgical operations in jaundiced patients are under consideration. In protracted and severe cases there is a marked tendency to subcutaneous, submucous, and subserous hemorrhages. The alkalinity of the blood is but slightly changed, if at all, except perhaps in some cases of cirrhosis with jaundice, in which it may be somewhat reduced. Whipple and Hooper<sup>3</sup> believe that in dogs, at least, hemoglobin can be rapidly changed into bile pigment in the circulating blood without participation of the liver. This they showed by injecting intravenously red cells from the same dog after they had been laked with distilled water. There was bile-pigment formation notwithstanding the fact that the dog's liver, spleen and intestines had been shut out of the circulation.

*The Heart and Bloodvessels.*—Bradycardia is a characteristic feature of jaundice, especially of acute cases and those of short duration. The pulse rate may fall to 60, to 40, even to 21 (Frerichs) a minute, and it is subject to sudden fluctuations upon slight provocation. This has been attributed to a local inhibitory action of the bile acids on the cardiac muscle or ganglia; but recent investigations suggest that perhaps the action is on the central nervous system. In chronic cases the bile acids become much reduced in amount or disappear, or the cardiac muscle becomes accustomed to their influence, and the bradycardia usually lessens or disappears.

*The Urine and Other Excretions.*—In jaundice a considerable portion of the biliary derivatives is excreted in the urine, which, in consequence, is discolored yellowish, yellowish red, greenish, or greenish brown, depending upon the relative amounts of bilirubin, biliverdin (its oxidation product), or urobilin (its reduction product). These bile pigments may be found in the urine several hours, or even several days, before there is any obvious discoloration of the skin or visible mucous membranes. The urine often contains a number of hyaline, sometimes bile stained,

<sup>1</sup> *Jour. Exp. Med.*, New York, 1912, xvi, 758.

<sup>2</sup> *Semaine méd.*, Par., 1908, xxviii, 49.

<sup>3</sup> *Jour. Exp. Med.*, New York, 1913, xvii, 593.

casts, attributable to irritation of the convoluted and Henle's tubules provoked by excreting the bile pigments (which are not excreted by the glomeruli).

Urobilinuria<sup>1</sup> is commonly observed in disease of the liver. Urobilin as well as urobilinogen are formed in the intestine by the action of bacteria on bilirubin; they are absorbed and carried to the liver by the portal circulation. They are found in the urine especially when the liver is disordered, and in chronic disease of the liver they are believed by Edsall<sup>2</sup> to be significant of cirrhosis when there is no passive congestion, obstruction of the biliary ducts, or carcinoma. The occurrence of urobilinuria in cases of jaundice does not justify the designation "urobilin jaundice," since the cutaneous pigmentation is due to bilirubin and biliverdin.

Excretions other than urine also are stained in jaundice, such as the sweat (staining of the personal and bed linen), serous exudates and transudates, etc. The saliva, tears, mucus, and milk are not stained, unless a pathological inflammatory exudate be added to them. The sputum of complicating croupous pneumonia is stained, but not that of bronchitis.

*The Liver.*—Although it is quite impossible to study the bile during life, except in those cases in which biliary fistulæ have been made, it is probable that during the persistence of the biliary obstruction bile is formed in lessened amount (oligochoelia, hypochoelia). In some cases bile pigments appear to be formed in normal amount; in some cases they seem to be lessened. French authors have described a colorless bile, which is said to contain bile acids and cholesterin.

*Nervous System.*—Grave disturbances of the nervous system occur in many cases of jaundice; on the one hand, there are manifestations of depression, such as general neuromuscular weakness, asthenia, headache, vertigo, mental depression (that may progress to melancholia), insomnia, etc.; on the other hand, there are manifestations of irritation, such as severe headache, active delirium, coma, convulsions, etc. These manifestations are more common in cases of acute toxic or infectious jaundice (associated with fever) than in the more protracted cases of obstructive jaundice; but they may supervene in any case of jaundice and not uncommonly lead to the fatal issue. They are commonly described under the name *cholemia*, but it is difficult to separate from one another the symptoms due to bile acidemia, to interference with the detoxifying function of the liver, and to the initiating toxic or infectious process. The condition is not *cholemia* in a restricted sense, that is, it is not due to bile acidemia, since the symptoms may occur when bile acids are not in excess in the blood, as well as in cases of disease of the liver (such as cirrhosis) unassociated with jaundice. The condition is most likely an acid intoxication, due to disturbances of the detoxifying function of the liver, which may be brought about by disorganization of the hepatic parenchyma such as occurs in severe forms of toxic and infectious jaundice, acute yellow atrophy of the liver, phosphorus poisoning,

<sup>1</sup> Consult Hildebrant, *Ztschr. f. klin. Med.*, Berl., 1906, lix, 351. See also a complete discussion by Wilbur and Addis, *Arch. Int. Med.*, 1914, xiii, 235 (literature).

<sup>2</sup> *Univ. Penn. Med. Bull.*, Phila., 1904, xvi, 427.

Eck's fistula, starvation, diabetes, etc., or by an excessive formation of enterogenic toxins, the consequence of absence of bile from the intestine.

*Gastro-intestinal Tract.*—The absence of bile from the intestinal tract results, as a rule, in the passage of large, pale, grayish, slate-colored or clay-colored, pasty, fetid, acid stools. The pale color is due, in part only, to the absence of bile; in part it is due to the large amount of imperfectly digested fats, which may be increased from the normal 7 to 10 per cent. to as much as 80 per cent. Microscopically and chemically the fats are found to consist of free fatty-acid crystals and soaps (calcium and magnesium) of the higher fatty acids; neutral fats are present in very small amounts. Rarely pale or decolorized stools contain biliary derivatives in considerable amount—determinable by chemical examination; this occurs especially in disease of the pancreas attended by obstruction to the outflow of the pancreatic juice but unassociated with jaundice. The pale color of the feces in these cases is due to the large amount of fat,<sup>1</sup> and to the reduction of bilirubin to leuko-urobilin.<sup>2</sup> It is not always warrantable, therefore, to base on the color of the stools an opinion of the amount of bile that enters the intestine or of the degree of biliary stasis. The offensive odor of the stools is usually ascribed to the absence of bile which, when present, limits fermentation of the intestinal contents. Often, however, there is very little fermentation. Strasburger has demonstrated no undue protein decomposition; and the odor may be described as peculiar rather than offensive, being due to the higher fatty acids. Rogers<sup>3</sup> believes that the bile acts not by neutralizing toxins but by hindering their formation. Constipation is perhaps the rule, and is due to defective motility, the result of lack of the stimulating influence of the bile. Sometimes the bowel movements are frequent, perhaps diarrhœic, which may be due to large fecal masses resulting from imperfect digestion of fat and to the laxative action of the free fatty acids. There is no effect on carbohydrate metabolism and very little on protein metabolism. Gastric hyperacidity is the rule, the biliary obstruction apparently causing an increase in the secretory activity of the stomach.

*General Nutrition.*—Man is able to withstand the effects of jaundice for a long time. The fatalities that ensue in the acute as well as in the chronic cases are due not so much to the jaundice *per se* as to other causes—the underlying cause of the jaundice, acid intoxication, etc. In long-standing cases, however, more or less disturbance of the general nutrition gradually ensues—due largely to imperfect fat absorption.

## ANOMALIES OF FORM AND POSITION

**Congenital Anomalies of Form.**—The liver, in consequence of defects of development, is occasionally found in the thoracic cavity or

<sup>1</sup> Consult Gordon, Cammidge, Watkins, and Robson, *Lancet*, Lond., 1905, ii, 1687, 1803, 1951; 1906, i, 57, 185, 255.

<sup>2</sup> Schmidt und Strasburger, *Die Faeces des Menschen*, 1905, 2te Aufl. 225.

<sup>3</sup> *Lancet*, 1910, i, 210.



projecting beneath the skin near the umbilicus (hepatomphalos); in monsters the organ may be entirely absent. Small portions of aberrant hepatic tissue are occasionally found in the suspensory ligament or the adjacent connective tissue. In partial and complete transposition of the viscera the liver may be as much in the left half of the body as normally it is in the right; in this event the left lobe is the larger. Rarely the normal relative size of the different lobes is changed: the left lobe may be unusually large or unusually small (defective blood-supply during intra-uterine or early extra-uterine life); the smaller lobes may be smaller or larger than normally, and they are sometimes more or less pedunculated. Congenital linguiform lobulation of the right lobe has been described; it is commoner in children, and it may be mistaken clinically for acquired linguiform lobulation. Well-marked lobulation of the entire organ is occasionally encountered: sometimes, doubtless, it is a fetal manifestation, homologous with similar lobulation of the kidney; often, however, it is a postnatal acquired condition due to syphilis, perhaps tuberculosis, perihepatitis, etc.

**Acquired Anomalies of Form (Deformities).**—The important acquired anomalies of form consist of: (1) The so-called corset, or constricted, liver; (2) linguiform lobulation; and (3) changes due to diseases of adjacent organs.

*The corset, or constricted, liver* is the consequence of tight lacing, and is therefore almost wholly confined to the female sex (as much as 25 per cent. of female cadavers in some series); but an analogous condition is sometimes encountered in men, the result of the constricting influence of a tight belt or strap. The basis of the deformity is a pressure atrophy of the liver parenchyma followed by fibrosis. Sometimes there is only a deep circumferential furrow; usually the liver is considerably elongated and markedly thinned at the point of greatest constriction (most marked atrophy), which often corresponds with the plane of the upper pole of the right kidney. In some cases but little hepatic parenchyma remains at the point of maximum constriction, and the elongated portion of the right lobe, which may reach to the transverse umbilical line, is attached to the major portion of the organ by a fibrous hinge-like band. Various grades of this condition are encountered, and it gradually merges into that spoken of as a linguiform (or Riedel's) lobe (partial hepatoposis). Occasionally the left lobe is similarly constricted and elongated. The surface of the superior part of the right lobe usually exhibits furrows or indentations corresponding with the ribs; occasionally the posterior margin of the left lobe is much infolded (corresponding folds of the diaphragm are usually encountered). The capsule of the liver and the overlying peritoneum are often much thickened, especially at the point of greatest pressure and constriction.

*Linguiform lobulation* is in many respects an exaggeration of the condition previously described. Both are common in female subjects, but the linguiform lobe, as originally pointed out by Riedel (whence Riedel's lobe) is intimately related to cholelithiasis and cholecystitis, enlargement of the gall-bladder being found in 60 per cent. of the cases. Tight lacing, however, is often at least partly responsible for the condition, since it

doubtless leads to kinking of the cystic duct and consequent obstruction to the free flow of bile. These linguiform lobes are often long and much attenuated; frequently they are attached to the main portion of the liver by a thin fibrous band; and they are often extremely mobile (partial hepatoptosis). In consequence of long-continued congestion they not infrequently show the lesions of well-marked nutmeg liver with increase in fibrous tissue. They are comparatively commonly the seat of other diseases, such as gumma, abscess, tumor, etc.

**Symptoms.**—The corset liver and a linguiform lobe may be entirely symptomless. In some cases there are symptoms of indigestion, as likely due to the tight lacing as to the changes in the liver. A lingual lobe is sometimes painful and tender, due to congestion or associated cholecystitis and cholelithiasis; occasionally nausea and vomiting ensue, and have been attributed to interference with the functions of the pylorus and duodenum; occasionally pains of biliary colic occur. In other cases the abnormality may be mistaken for an abdominal tumor.

**Diagnosis.**—This is not specially difficult when the likelihood of the conditions is borne in mind and the abdomen is examined carefully. Usually the abnormal lobe will be found to move with the liver during respiration, and it can be proved to be continuous with the liver, even when a coil of intestine courses over the most constricted part. The lobe may be mistaken for a dilated gall-bladder, floating kidney, hydro-nephrosis, tumor of the stomach, colon, pancreas, omentum, or ovary (solid or cystic), appendicitis, etc.

**Prognosis.**—The prognosis depends upon the etiological factors and the advance made by the lesions.

**Treatment.**—The corset liver is better prevented than cured.

**Acquired Anomalies of Position.**—The liver may be displaced upward, downward, or laterally, or it may be rotated on its anteroposterior axis (anteverted or retroverted). Displacement downward results in consequence of disease above the diaphragm, such as pleuritis with exudation, hydrothorax, emphysema, tumors or abscesses of the lungs or mediastinum, etc., as well as of disease between the diaphragm and the liver, subdiaphragmatic or suprahepatic abscess. Displacement upward results in consequence of disease of the abdominal organs, especially ascites, tympanites, tumors, traumatic diaphragmatic hernia, etc. Frequently when displaced upward the liver is also rotated posteriorly, so that the inferior surface presents anteriorly and upward, due to the liver being rather fixed posteriorly with the inferior vena cava. Occasionally the liver is tilted anteriorly, so that much of the upper surface of the organ comes in contact with the anterior abdominal wall; its anterior edge may fall as low as or lower than the umbilicus, whence marked enlargement of the organ may be simulated. This may occur in large aneurism of the descending thoracic or upper abdominal aorta, and in tumors of the kidney, adrenal, retroperitoneal glands, etc. The *symptoms* of such displacement of the liver are altogether secondary to those due to the primary disorder. The *diagnosis* is usually quite obvious upon detecting the primary disorder; indeed, in some cases the evident displacement of the liver is a valuable aid in recognizing the primary disorder (such

as pleural exudation, etc.). The displacement must be differentiated from other diseases, causing, on the one hand, lessening of the liver dulness and apparent diminution in the size of the liver (acute yellow atrophy, portal cirrhosis, intestinal distension, etc.), and those, on the other hand, causing enlargement of the liver (fatty and amyloid degeneration, portal and biliary cirrhosis, leukemic infiltration, carcinoma, sarcoma, etc.).

**Hepatoptosis.**—The important acquired anomaly of position is that variously spoken of as hepatoptosis, wandering liver, movable liver, etc., a condition in which the liver is abnormally movable and presents variously in the abdominal cavity.

### DISEASES OF THE HEPATIC ARTERY

**Dilatation.**—This occurs when the portal vein is obstructed (thrombosed or compressed), in which event the artery acts vicariously for the vein; this is seen especially when small branches of the portal vein are obstructed. The dilatation involves usually the branches of the hepatic artery, but it may extend to the main trunk. This compensatory action of the artery for the vein is never efficient. A compensatory enlargement of the hepatic artery is observed also in conditions of connective-tissue overgrowth, as in the advanced stage of cirrhosis. The capillaries especially are involved, but the process may extend to the main trunk. This is an important factor in causing the increased portal pressure and the consequent ascites in portal cirrhosis.

**Thrombosis.**—Thrombosis of the hepatic artery in man is such a rarity, not more than two cases (Ledien and Lancereaux) being on record, and one of these being doubtful, that its results are unknown.

**Embolism.**—Embolism of the hepatic artery is comparatively uncommon. Purely mechanical emboli are probably comparatively innocuous, on account of the free arterial anastomosis, and the part of the organ cut off from blood-supply by embolism of a small branch of the hepatic artery is doubtless speedily supplied by blood from a collateral vessel. Embolism of the main trunk or principal branch has resulted in anemic infarction and necrosis. Infectious emboli are not rare; they occur in sepsis, involve the smaller branches of the artery, and give rise to multiple abscesses. Clinically the general condition usually overshadows the local lesions in the liver. Sarcomatous emboli are often observed in melanotic sarcoma, especially that originating in the eye.

**Aneurism.**—Aneurism of the hepatic artery is a rare condition. Rolland<sup>1</sup> in 1908 was able to collect from the literature only 40 undoubted cases. The condition is about three times as common in men as in women (30 men, 9 women, Rolland). The age varies from fourteen to eighty-three years, the average of 36 cases being thirty-seven years; the average in men being thirty-five years, in women forty-five years (Rolland).

**Pathology.**—The aneurism may be extrahepatic or intrahepatic. Of the 40 cases collected by Rolland, 24 were extrahepatic, 8 intrahepatic,

<sup>1</sup> *Glasgow Med. Jour.*, 1908, lxi, 342.



2 both extrahepatic and intrahepatic (two aneurisms in each), and 6 were not definitely described. In Rolland's own case there were three aneurisms, all intrahepatic. In 16 cases the main vessel was involved; in 12, the right branch; in 3, the left branch; in 3, both branches; and in 1, the cystic artery. The aneurism may be of the true or the false variety. Of the 40 cases collected by Rolland, 32 resulted in rupture into the peritoneum, the biliary passages, the portal vein, the stomach, the duodenum, with associated rupture of the liver in the intrahepatic forms in 4 cases; 6 were found unruptured; and in 2 the condition is not known.

**Symptoms.**—Rolland states that the three most constant symptoms are pain, jaundice, and hemorrhage. Pain is rarely absent; in typical cases it is paroxysmal and resembles that of biliary colic, being referred to the right hypochondrium and epigastrium, which are usually tender. Pain is usually absent between attacks. The pain is attributed to pressure on the hepatic plexus of nerves and to stretching of Glisson's capsule. Jaundice occurred in 16 of the 40 cases; but in most of the cases there is no statement with regard to jaundice. When present it has usually been more or less permanent, and is due to pressure on the hepatic or the common bile duct. In none of the cases did the jaundice appear to be related to the attacks of pain. Hemorrhage into the alimentary tract occurred in 17 of the 40 cases. Usually the blood reached the alimentary tract by way of the biliary ducts; rarely was there direct hemorrhage into the stomach or the duodenum; and rarely the bleeding was due to pressure on the portal vein and consequent passive congestion. Melena is the common clinical symptom; hematemesis is less common. The hemorrhage may be frequently repeated. Fever (as high as 104°) occurred in a few cases, usually with the paroxysmal pain, and was sometimes accompanied by rigors. Disturbances of digestion are common, due to the effect of local pressure by the aneurism.

**Diagnosis.**—No case has been recognized during life except at exploratory laparotomy—whereby Kehr first detected the condition. Cholelithiasis and duodenal ulcer are the most likely diagnoses. Hemorrhages are much less frequent in cholelithiasis than in aneurism of the hepatic artery; in aneurism hemorrhage may be the first symptom; in cholelithiasis it is always a late symptom, usually due to fistula formation; both conditions may occur together. The association of symptoms of duodenal ulcer and of biliary colic might suggest the diagnosis.

**Treatment.**—Should the condition be diagnosed, the hepatic artery or one of its branches should be ligated. This has been done successfully by Kehr, and is justifiable, since a sufficient collateral circulation is likely to develop. Otherwise treatment is purely palliative.

## DISEASES OF THE HEPATIC VEINS

**Dilatation.**—Dilatation of the hepatic veins and their branches is a concomitant of disease of the heart and lungs attended by failure of the right side of the heart. The dilatation extends to the central vein of the hepatic lobule, and is often associated with thickening of the vessel wall,

perivascular fibrosis, and pigmentation and atrophy of the surrounding hepatic parenchyma.

**Thrombosis.**—Thrombosis of the hepatic veins is a rare condition due to: (1) Intrahepatic or extrahepatic compression of the vein or its branches by a tumor, cyst, enlarged glands, etc.; (2) chronic stricture, the consequence of adhesions (perihepatitis) near the junction of the inferior vena cava; (3) neoplastic invasion of the vessel wall, which may progress to penetration of the vessel wall; (4) acute and chronic inflammatory disease of the vessel wall, syphilis, tuberculosis, etc., usually associated with interstitial hepatitis; (5) extension of a clot partially or completely occluding the inferior vena cava; and (6) occasionally it follows, sometimes precedes, thrombosis of the portal vein. The lesions are analogous to those of chronic passive congestion. Ascites and more or less enlargement of the spleen usually develop rapidly, but the condition is scarcely susceptible of clinical recognition. It may be suspected in cases of aggravated passive hyperemia upon the sudden onset of ascites.

**Embolism.**—Embolism of the hepatic veins is uncommon, and can result only from reversal of the blood stream.

**Suppurative Phlebitis.**—Suppurative phlebitis (thrombophlebitis) of the hepatic veins sometimes ensues in cases of acute infectious inflammation of the liver, suppurative cholangitis, hepatic abscess, etc., the infection being more prone to involve the hepatic veins than the branches of the portal vein, because the latter are comparatively well protected by a connective-tissue capsule. In the event of suppurative phlebitis of the hepatic veins, secondary abscesses in the lungs and general septicopyemia ensue.

**Chronic Obliterating Endophlebitis.**—Chronic obliterating endophlebitis of the hepatic veins, a disorder characterized by slow proliferation of the lining of the hepatic veins and consequent obstruction, is a comparatively rare affection. Hess<sup>1</sup> in 1905 was able to collect only 23 cases, but he is inclined to believe that many cases have been overlooked, since clinically they resemble ordinary or portal cirrhosis of the liver, and unless at the necropsy the hepatic portion of the inferior vena cava is opened and the ostia of the hepatic veins examined, the clinical diagnosis of cirrhosis of the liver is likely to be declared correct.

### DISEASES OF THE PORTAL VEIN

**Thrombosis.**—Thrombosis of the portal vein (pylethrombosis, pylephlebitis adhesiva) is more common in males than in females. It occurs at all ages, the average age in men being 44.8 years, and in women 41 years (Rolleston). The thrombosis may begin in the portal radicles within the liver, in the main trunk of the vein, or in the peripheral radicles anywhere within the area of collection of the vein; and subsequently by extension the process may become widespread.

*Thrombosis of the intrahepatic radicles of the portal vein* is the commonest form, and is due most frequently to cirrhosis. The cirrhotic process

<sup>1</sup> *Amer. Jour. Med. Sci.*, 1905, cxxx, 986.

leads to gradual obstruction and ultimate isolation of certain sections of the portal distribution, and the increased pressure induces endophlebitis, in consequence of which the contained blood coagulates. The original coagula are gradually increased in size by secondary accretions, until not infrequently they become widespread, extending even to the main trunk of the portal vein. Thrombosis within the branches of the portal vein in the liver is also found in conditions that impede the local circulation, such as failure of the general circulation by whatever cause induced; inflammatory disorders (cholangitis, cholelithiasis, liver abscess, etc.); secondary new-growths, syphilis, etc.; in these conditions, however, the coagula, as a rule, are recent and of little clinical interest.

*Thrombosis of the main trunk of the portal vein* usually results from slow chronic inflammatory and degenerative processes in the wall of the vein (endophlebitis, phlebosclerosis, calcification), which in turn may be set up by a variety of processes. It may be a part of the cirrhotic process; it may be associated with chronic inflammatory process in its vicinity, that is, in the lesser omentum and peritoneum (thickening and induration, causing kinking and constriction of the vein), in the stomach and duodenum (ulcers with surrounding inflammatory induration), in the pancreas (swelling and induration compressing and distorting the vein); it may be due also to malignant and other new-growths of the stomach, intestine, pancreas, etc. The primary growth or the metastasis to regional lymph glands (hilum of the liver, retroperitoneum, mesentery, etc.), may implicate the main trunk or one of the larger branches that go to form it, and by compression, distortion, or invasion set up thrombosis. The thrombus may extend and become very extensive.

*Thrombosis of the peripheral radicles that go to form the portal vein* may be induced by inflammatory or neoplastic disease in any one of the organs of the gastro-intestinal tract, the spleen, the female genitalia, etc., that lead directly or indirectly to the portal vein. The primary coagula often increase in size until they reach the main trunk; or small portions may be detached and carried to the liver, causing embolism and more or less extensive secondary thrombosis.

The most frequent causes of thrombosis in any or all parts of the portal vein are cirrhosis of the liver and intra-abdominal new-growths. There is this interesting fact in connection with these thromboses: although they commonly do not undergo suppuration, bacteria not infrequently can be cultivated from them. This suggests that bacteria of attenuated virulence may be concerned in their formation, although of course one cannot exclude the possibility of secondary infection. It is not unlikely, however, that in at least some cases the bacteria set up a primary low-grade phlebitis, whereupon thrombosis follows.

**Pathology.**—The thrombus may be recent or old; not infrequently it is both: the one part pale, firm, fibrous, and intimately adherent to the wall of the vein; the other reddish, soft and readily detached. It may completely or only partially occlude the lumen of the vein; or in the same case in one place it may completely and in another partially obstruct the lumen; that is, it may be annular, parietal, channelled, etc. The portal vein is usually thickened (phlebosclerosis); it not infrequently



contains calcareous plates; and it may be represented by a firm, non-channelled fibrous cord (stricture or complete stenosis). Peripherally to the thrombus the portal vein is much dilated and tortuous, and a collateral circulation, analogous to that of cirrhosis of the liver, usually becomes established.<sup>1</sup> The liver presents the primary condition and sometimes, in addition, dilatation of the hepatic artery (compensatory), infarction, fatty degeneration, softening, necrosis, perhaps some fibrosis, etc. When there is thrombosis of the main trunk of the portal vein, or of the splenic vein, the spleen is enlarged and may show infarction. When the main trunk or the mesenteric veins are thrombosed, the small intestine shows hemorrhages and infarction, which may proceed to gangrene; this is usually most marked in the middle of the jejunum, which has no collateral circulation.

**Symptoms.**—Thrombosis of the portal vein may be entirely latent, that is, occurring usually in the course of other disorders; the manifestations of the primary condition usually entirely overshadow those due to the thrombosis. Sometimes, however, to the symptoms of the primary disorder others are added that may suggest the diagnosis. In about 60 per cent. of the cases (Langdon Brown)<sup>2</sup> the onset is acute; that is, although the thrombosis may be a gradual process, symptoms due to complete obstruction develop suddenly. The most marked consist of ascites, enlargement of the spleen, and various disorders of the gastro-intestinal tract. Ascites is present in 65.6 per cent. of the cases (Rolleston); it may be absent in cases that speedily terminate fatally, in those in which the mesenteric veins are involved chiefly or alone, and in certain cases of long standing in which an efficient collateral circulation has been established. As a rule the ascites develops rapidly, becomes extreme, and speedily reaccumulates after removal. The spleen is usually enlarged, often enormously engorged; but ascites and tympanites may prevent its ready recognition, and perisplenitis with adhesions may prevent enlargement. The spleen often decreases notably in size after gastro-intestinal hemorrhage. Of the gastro-intestinal symptoms, the most important are various dyspeptic symptoms, vomiting, hematemesis, and intestinal hemorrhage in 44.2 per cent. of cases (Rolleston), diarrhoea (serous or serosanguinolent, due to increased venous pressure), symptoms of intestinal obstruction (paralysis due to hemorrhagic infarction), hemorrhoids, etc. The abdomen may reveal dilated veins. The general condition is poor; the appetite, strength, and flesh fail; the urine lessens in amount (due to lowered blood-pressure); anemia, cedema, and finally cachexia supervene; and not infrequently phenomena of toxemia suggesting uremia appear, and the patient dies.

**Diagnosis.**—In most cases this is impossible, but it is suggested by the sudden onset of marked ascites, gastro-intestinal hemorrhage, enlargement of the spleen, abdominal pain, and symptoms of intestinal obstruction. When the intrahepatic branches or the main trunk of the portal vein are involved the disorder can scarcely be differentiated from cirrhosis, with which it is often associated; but a very acute onset suggests

<sup>1</sup> Consult Pick, *Arch. f. path. Anat.* (etc.), *Berl.*, 1909, cxcvii, 490 (literature).

<sup>2</sup> *St. Barth. Hosp. Rep.*, 1901, xxxvii, 62.

the thrombosis. Unusual enlargement of the spleen and copious hematemesis suggest involvement of the splenic vein; diarrhœa (serous or serosanguinolent) or abdominal pain, bloody stools, and symptoms of intestinal obstruction suggest involvement of the mesenteric veins.

**Prognosis.**—Many subjects die soon after the development of the thrombosis; the prognosis therefore is bad. In some cases, the process being gradual, a more or less efficient collateral circulation is established, which may prolong life for some time; in this event the duration depends largely upon the primary disorder, but it is rarely more than two years.

**Treatment.**—This is purely palliative, and resolves itself into that of serious hemorrhages and of ascites; the ascites usually requires repeated tapping. Measures to prevent thrombosis in cirrhosis and in other conditions in which it may supervene, or to limit it when it has developed (providing it can be recognized), are of theoretical interest. Operative intervention, with a view to promote the formation of adhesions about the liver, or to remove the obstruction in the portal vein, is scarcely feasible. Curtis<sup>1</sup> has suggested splenectomy.

**Embolism.**—Embolism of the intrahepatic branches of the portal vein is a rather common sequence of inflammatory, suppurative, ulcerative, and neoplastic processes of the organs within the area of collection of the portal vein. The most common antecedents of such embolism are appendicitis (with suppuration or ulceration and thrombosis of its veins), ulcerative processes of the intestine, notably dysentery, and tumors of the gastro-intestinal tract; but embolism occurs also in divers disorders in which thrombosis of the hemorrhoidal, mesenteric, gastric, or splenic veins develops. The emboli usually are small, and they are of significance largely on account of the conditions in the liver to which they may give rise, notably multiple liver abscesses, or secondary neoplastic deposits.

**Suppurative Pylephlebitis.**—Suppurative pylephlebitis (portal pyemia) is more common in males than in females; it is especially common in early adult life, coinciding with the age incidence of appendicitis. Like adhesive pylephlebitis, it may begin in the portal radicles within the liver, in the main trunk of the vein, or in the peripheral radicles anywhere within the area of collection of the vein; and subsequently by extension the process may become more or less widespread. Usually the process begins in the peripheral radicles, being secondary to ulcerative and suppurative processes of the gastro-intestinal tract. Of these the most common is ulcerative or suppurative appendicitis, more particularly in cases neglected surgically, or in which infectious thromboses occur in the appendicular and the mesenteric veins. Less commonly ulcerative and neoplastic processes of the stomach and intestines, such as gastric and duodenal ulcer, typhoid, tuberculous and dysenteric ulceration of the intestine, gastro-intestinal carcinoma, fissures, ulcer and strictures of the rectum and anus, suppurative or gangrenous pancreatitis, suppuration of the mesenteric glands, suppurative disease of the female genitalia, abscess of the spleen, etc., constitute the starting-point of the infective thrombosis. Occasionally, also, the process originates in operative

<sup>1</sup> *Proc. Roy. Soc. Med.*, Lond., (Path. Sect.), 1909, ii, 159.

infection of the mesenteric radicles of the portal vein (operations on the intestine). The thrombus occasionally begins in the main trunk of the vein, sometimes in consequence of operative trauma, but usually secondarily to a local focus of suppuration—perigastric, periduodenal, subhepatic, etc.; or to gall-stones in the common duct, with surrounding suppuration, etc. Suppurative pyelephlebitis rather rarely begins within the liver, but it may be sequential to a liver abscess, suppurating hydatid cyst, suppurative cholangitis (with or without cholelithiasis or cholecystitis), etc. In these cases the infection is much more likely to involve the hepatic rather than the portal vein, since the latter is protected by a connective-tissue envelope; but infection of the portal vein does occur, doubtless by the lymphatics, although sometimes by continuity.

**Pathology.**—The process may be more or less localized or quite widespread. Usually the peripheral radicles and some of the main branches of the vein are involved; sometimes the process involves also the main trunk and extends into the liver; in some cases the peripheral radicles and the ramifications in the liver are implicated, the main trunk being almost if not quite free; in this event the intrahepatic lesions are embolic. The vein is enlarged, swollen, softened, congested, œdematous (panphlebitis); it is filled with a more or less softened (necrotic) sanguinolent-purulent or purulent material partially or completely obstructing the lumen. When not entirely liquefied the clot is more or less friable, occasionally free in the lumen, but usually it is more or less intimately attached to the intima. Not infrequently there is obvious purulent infiltration of the wall of the vein, and a sheath of pus or purulent material about the vein (perivascular lymph spaces) and in the adjacent connective tissue, usually on the right side. The liver is usually enlarged and contains foci of necrosis or multiple abscesses; the spleen is enlarged and softened; not infrequently there is localized or generalized purulent peritonitis; there may be a purulent pleuritis; and sometimes secondary abscesses develop in different regions of the body.

**Symptoms.**—Since suppurative pyelephlebitis is a secondary disorder, the symptoms directly attributable to it are preceded by those of the disease to which it owes its origin, notably appendicitis. The onset of the pyelephlebitis is usually sudden, and is manifested by the phenomena of septicopyemia: irregular chills, fever, and sweats, a soft, compressible, rapid pulse, leukocytosis, and general prostration. To these may be added extension of the abdominal pain beyond the seat of original disease, enlargement and tenderness of the liver (about one-half of the cases), enlargement of the spleen (one-fourth of the cases), etc. Vomiting, hematemesis, and diarrhœa are sometimes observed. Symptoms referable to various complications (pleuritis, brain abscess, etc.) may supervene.

**Diagnosis.**—This rests upon an obvious primary cause, the development of a septicopyemic state, and evidences of involvement of the liver (enlargement, tenderness, and perhaps slight jaundice). In the differential diagnosis one has to consider other forms of liver abscess and of septicopyemia, typhoid fever, etc.

**Prognosis.**—The disorder is fatal in the great majority of cases, especially when the main trunk of the vein is involved or when there are multiple abscesses in the liver.



**Treatment.**—The disease is much easier prevented than cured. Appendicitis should be promptly treated surgically, and other ulcerative or suppurative conditions of the gastro-intestinal tract should be appropriately treated, so as to prevent the formation of infectious emboli. When developed the treatment of pylephlebitis is that of liver abscess.

**Chronic Endophlebitis.**—Chronic endophlebitis, a process allied to arteriosclerosis, apparently may be primary or secondary. The primary process is exceptionally rare, and its etiology is ill understood; doubtless some cases are due to syphilis; in splenic anemia, hyperplastic changes initiated in the endothelium of the blood-sinuses of the spleen may gradually spread to the splenic and the portal veins, and ultimately involve the portal radicles in the liver; to this is attributed the sequential cirrhosis of the liver (Banti's disease with cirrhosis of the liver). Secondary endophlebitis of the portal vein is encountered in cirrhosis of the liver, and in advanced passive congestion. In these cases it is usually attributed to the increased pressure, but in many cases toxic products doubtless play a part. Partial or complete thrombosis may follow chronic endophlebitis; and calcification not uncommonly ensues.

## RETROGRESSIVE DISORDERS OF THE LIVER

**Atrophy of the Liver.**—This is a term more or less generally but inaptly applied to conditions in which the liver becomes reduced in size. Most of these conditions are degenerative and not truly atrophic.

*Localized atrophy* occurs under most diverse circumstances, generally in consequence of pressure, such as tight lacing, or belts, deformities of the chest and vertebræ (kyphosis and scoliosis), tumors and other disorders of adjacent organs, etc.; it occurs also in certain diseases of the liver itself, such as in the vicinity of tumors and cysts, in consequence of the occlusion of a branch of the portal vein or hepatic artery, and in passive congestion, amyloid disease, cirrhosis, etc. Under these varying circumstances there is a more or less localized reduction in the size of the liver, which may be: (1) Truly atrophic with subsequent replacement fibrosis, as in pressure exerted by corsets or other constrictions, etc.; or (2) atrophic and degenerative (especially fatty degeneration and necrosis), as in passive congestion, amyloid disease, cirrhosis, etc.

*General atrophy* may follow stenosis or occlusion of the portal vein; general hepatitis with thickening of the capsule; advanced cirrhosis, advanced passive congestion, etc.; and a reduction in the size of the liver, which, however, is not a true atrophy, follows many widespread degenerative processes, such as acute yellow atrophy, and poisoning by phosphorus, arsenic, chloroform, etc. A decrease in the size of the liver, to which the term atrophy is truly applicable, occurs in conditions of general wasting, as in senile atrophy inanition, certain cachexias, etc. The liver becomes reduced in size, because of a reduction in size and possibly also in number of the liver cells, without degenerative changes in the hepatic parenchyma or noteworthy changes in the inter-

stitial tissues. In senility the liver participates in the general atrophic process. Otherwise this general atrophy of the liver is due to disturbances of metabolism brought about by: (1) Deficient nourishment, or inability to utilize available food, as in obstruction of the œsophagus, etc.; or (2) excessive drain and waste attendant upon malignant growths, protracted suppuration, etc.

**Pathology.**—The liver is reduced in size, dark in color, dense, flaccid, of increased specific gravity, and dry—changes attributable to disappearance of the parenchyma and relative increase of the connective tissue. The section surface is dry, and the acini are obviously reduced in size and perhaps in number. These changes, although widespread, are not uniform, the margins, as a rule, being relatively more affected than the central portion of the lobes. The liver cells are reduced in size and number, and often contain considerable pigment.

**Symptoms.**—The symptoms are those of the primary disorder.

**Parenchymatous Degeneration.**—This (cloudy swelling) is perhaps the commonest deviation from the normal exhibited by the liver. To some extent it is a physiological process and is seen when excessive demands are made upon the liver. Otherwise cloudy swelling results from the action of divers poisons, bacterial and non-bacterial. The process is especially common in the infectious diseases, notably typhoid fever, pneumonia and dysentery. The liver is enlarged, somewhat softened, of lessened elasticity, pale, somewhat dull and opaque (as though cooked), and on microscopic examination reveals swelling, increased granulation and opacity of the liver cells, and obscuration of the nuclei. The condition is of secondary clinical interest, being only a part of general toxemic processes. Clinically some enlargement and occasionally tenderness of the liver may be elicited.

**Gaseous or Emphysematous Liver.**—This is characterized by numerous gaseous cysts in the liver due to *Bacillus aerogenes capsulatus*. The infection is rarely primary, although the organism has been cultivated from the blood before death; usually it is secondary, and occurs at or about the agonal period or after death from other causes. The organism is usually found in association with other bacteria, and although present before death, the gas formation is a postmortem phenomenon. The liver is most commonly involved, but the process may be widespread. The infection usually occurs by way of the portal vein (from the intestinal tract); but it may occur by way of the general circulation, or directly from the intestine to the biliary ducts and the gall-bladder. The liver is enlarged, soft, and spongy, and is pervaded by numerous usually small gaseous cysts. The condition is chiefly of pathological interest, and is not susceptible of clinical recognition.

**Fatty Liver.**—This is a comprehensive term applicable to the different conditions characterized by an excess of fat in the liver. On the one hand it includes fatty infiltration, in which there is an excessive deposit of fat in otherwise unaltered or slightly altered liver cells; and on the other hand, fatty degeneration, in which in addition to the fat there are greater or less degenerative changes in the hepatic parenchyma, perhaps the direct conversion of the liver cells into fat. Formerly the

two conditions were differentiated; doubtless there are extreme cases of fatty infiltration and of fatty degeneration, but many cases partake of the nature of both processes, and there is considerable evidence that the fat in the liver under all circumstances is derived mainly from adipose tissue elsewhere in the body; that even in phosphorus poisoning the fat in the liver is not due, wholly at least, to conversion of the liver protein.<sup>1</sup> It seems impracticable, therefore, to differentiate fatty infiltration sharply from fatty degeneration; both processes are appropriately discussed as fatty liver, or fatty changes in the liver.

**Etiology.**—The causes are: (1) Dietetic indiscretions and associated disorders of metabolism, notably the ingestion of too much food, particularly fat and carbohydrates, to which is usually added a sedentary life and lack of muscular exercise and of mental activity—factors that, combined, tend to produce obesity, of which fatty liver (mostly infiltration) is a conspicuous feature. The fatty deposit is ascribed to incomplete oxidation of the excessive amount of food. (2) Anemic and cachectic conditions, such as occur in the late stages of many chronic disorders, such as tuberculosis, carcinoma, etc., in which in consequence of deficient supply of blood there is deficient oxidation; but the influence of toxic substances may not be ignored. (3) Passive congestion due to a variety of causes that lead to failure of the heart—in which the fatty infiltration of the periphery of the liver lobules is in marked contrast to the congested centres (nutmeg liver). (4) Poisons of most diverse nature, notably chronic alcoholism. Alcohol seems to be a definite protoplasmic poison to the liver cells, and in addition to taking oxygen for its own combustion, gives rise to deficient oxidation of other food products. The fatty changes are often associated with cirrhosis (fatty cirrhosis). Other poisons causing fatty changes are minerals, such as phosphorus, arsenic, mercury, etc.; mineral acids, such as hydrochloric, nitric, sulphuric, etc.; and other chemicals, such as chloroform, iodoform, carbolic acid, phloridzin; fungi, meat poisons, etc. (5) Certain local infections of the intestinal tract, such as the gastro-intestinal catarrh of children, dysentery, etc., in which toxins are carried to the liver by the portal vein. (6) Certain general infections, notably streptococcic and staphylococcic and other pyococcic infections of long duration (prolonged suppuration), tuberculosis, etc. The exact cause of the fatty liver that occurs in about one-third of the cases of tuberculosis is not well understood, although doubtless it is in some way related to deficient oxidation.

**Pathology.**—Usually the liver is enlarged and may weigh 3000 to 4000 grams; it is of lessened specific gravity (sometimes floating in water), and of lessened resistance; it is normal in conformation, and has a smooth surface and rounded edges, and is pale yellowish in color. The section surface is usually pale, anemic, obviously fatty; in cases of passive congestion the well-known appearances of nutmeg liver (dark centre and light periphery of the lobules) are seen; and in fatty cirrhosis the association of fibrosis is obvious. Histologically the cells at the periphery of the lobules contain fat droplets that vary much in

<sup>1</sup> Adami, *Principles of Pathology*, 1911, i, 430 and 905.



size and displace the cellular protoplasm and nuclei, which otherwise are not notably altered; after removal of the fat the cells may revert to their normal condition. Fatty degeneration may involve any part of the liver lobule but is most often in the central zone;<sup>1</sup> the cells reveal minute droplets of fat throughout the protoplasm, which otherwise is markedly granular, distorted, and opaque; the nuclei, at first unaltered, soon undergo retrograde change; after removal of the fat the cells are shrunken, opaque, and evidently the seat of retrograde metamorphosis.

**Symptoms.**—These are ill-defined. It is important to bear in mind that such symptoms as may be present are due to the initiating disease and the degenerative change in the liver cells rather than to the mere presence of fat. In general the symptoms are those of the primary disorder, obesity, tuberculosis, alcoholism, etc. In perhaps the majority of cases there are no symptoms referable directly to the liver; occasionally sensations of weight may be due to the mere weight of the liver, and ill-defined dyspeptic symptoms may be attributed to functional inactivity of the liver, although they are more likely to be due to associated disorders of the stomach and intestines, improper eating and drinking, etc. The liver is enlarged and commonly palpable two or three finger-breadths below the costal margin; excessive fatty deposit in the abdominal wall, as well as the flaccidity of the liver itself, may render the examination unsatisfactory. In thin tuberculous subjects the enlarged liver, however, is usually readily palpable. In associated cirrhosis and amyloid disease, etc., the liver is usually firm and more readily palpable.

In phosphorus poisoning the early symptoms are those of gastrointestinal irritation (epigastric distress, nausea, and vomiting). If the patient does not die soon, there is commonly a period of quiescence that to the unwary suggests recovery and speedy cure. At the end of two or three days, however, vomiting and epigastric distress return, jaundice supervenes, the pulse becomes weak and accelerated, the heart dilated, hemorrhages appear and the patient usually dies within a week. In most cases the liver is enlarged throughout, smooth and tender; in some cases it decreases in size before death.

**Diagnosis.**—Minor grades of fatty liver cannot be recognized with certainty; the more marked grades must be differentiated from other causes of enlargement. The fatty cirrhotic liver occasions the symptoms of cirrhosis, notably hematemesis, ascites, and enlargement of the spleen, which do not belong to the fatty liver. The amyloid liver is much firmer than the fatty, has a more or less obvious cause, and is associated with amyloid disease elsewhere. Leukemic enlargement of the liver is readily recognized by the blood examination. The enlarged liver of passive congestion is readily determined by recognizing an obvious cause. A displaced liver should be recognized by a careful examination. The liver of phosphorus poisoning should be determined by the history, general phenomena, and the subsequent development of jaundice, which does not occur in other forms of fatty liver.

**Prognosis.**—The prognosis depends upon the primary cause.

<sup>1</sup> McCrae and Klotz, *Jour. Exp. Med.*, 1910, xii, 746.

**Treatment.**—The treatment is altogether that of the primary disorder, obesity, alcoholism, etc., of which, from a therapeutic point of view, the fatty liver usually constitutes an almost negligible associate.

**Amyloid Degeneration.**—This is a process characterized by the conversion of the proteins of the tissues into a structureless homogeneous substance called lardacein.

**Etiology.**—Amyloid degeneration is a disease of young male subjects (usually less than thirty years); but sex and age are probably only of significance as the common antecedents of amyloid degeneration are most common in young males. In the great majority of cases it follows prolonged suppuration, especially that due to syphilis and tuberculosis and involving the bones and the lungs. Less commonly it occurs in the absence of suppuration, as in the cachexia of tertiary syphilis, chronic malaria, malignant disease, and in delayed convalescence from infectious diseases. In most cases the direct cause seems to be the absorption of the toxic products of pyogenic cocci. Most of the cases occur in association with ill-drained cavities, from which toxic absorption is continuous and considerable.

**Pathology.**—The relative frequency of involvement of the different organs is shown by the combined statistics of Birch-Hirschfeld, Loomis, Dickinson, Goodhart, and Turner. Of 795 cases the spleen was involved in 585, the kidneys in 539, and the liver in 387 (Rolleston). The amyloid liver is enlarged, sometimes to four or five times its normal size; its general conformation is preserved, its edges are sharp or slightly rounded, and its surface smooth; it is pale in color, firmer than normal, of increased specific gravity and lessened elasticity. The section surface is smooth, pale, grayish red in color, and peculiarly translucent, glistening, or bacony in appearance (especially apparent at the edge of the cut surface). In minor grades the individual lobules are more or less obvious, but later they lose their identity. A fresh cut surface treated with iodine strikes a mahogany-brown color, which occurs in more or less ring forms in the mid-portion of the lobules, the remaining portions (centre and periphery) of the lobules being pale yellowish or yellowish brown. Microscopically, the amyloid material is first found in the subendothelial layer of the capillaries of the mid-zone of the liver lobules; later it involves other capillaries and arterioles and spreads to the media; still later similar changes occur in the small venules, and ultimately the process involves the adjacent connective tissue. On account of defective nutritive supply, and doubtless also in consequence of the direct action of toxins, the parenchymatous cells show cloudy swelling and fatty degeneration, and are ultimately removed or converted into amyloid material.

**Symptoms.**—These are those of amyloid disease in general—progressive emaciation, anemia, and debility, usually in a person the subject of chronic suppuration or syphilis. The liver is enlarged (it may reach much below the umbilicus), painless, smooth, firm, and has sharp or somewhat rounded edges. The spleen is usually enlarged and firm; often there are evidences of amyloid degeneration of the kidneys (polyuria, albuminuria, waxy casts, etc.), of the intestinal tract, (diarrhoea), and of the cardiovascular system (weak heart, low blood-

pressure, œdema, etc.). There is no jaundice or evidence of portal obstruction, except in the event of complications.

**Diagnosis.**—This is comparatively easy in some cases: a history of syphilis, or of long-standing suppuration, with enlargement of the liver and spleen, albuminuria, and perhaps diarrhœa, or weak heart and œdema, is quite unmistakable. Amyloid must be distinguished from other painless enlargements of the liver. The fatty liver is usually associated with obesity, alcoholism, etc., and the liver is softer. The fatty cirrhotic liver is likely to be tender, there are the antecedents of cirrhosis and its more common phenomena. Leukemic enlargement is readily recognized by a blood examination.

**Prognosis.**—This is bad, although some improvement may be effected; occasionally the liver becomes considerably reduced in size.

**Treatment.**—The essential part is to eliminate the cause; suppurative foci must be adequately drained and the suppuration stopped as soon as possible; syphilis should be appropriately treated. Attention to the general health is of the greatest importance, and comprises good food, fresh air, rest, hygienic surroundings, bitter tonics and alteratives, syrup of iron iodide), etc.

**Pigmentation of the Liver.**—This occurs under a variety of circumstances, but in itself is of comparatively little clinical importance. Certain extraneous pigments are sometimes found, such as coal-dust (anthracosis), stone-dust (silicosis), silver (after medicinal administration), etc. The associated changes are usually those of slight or moderate fibrosis, to which perhaps the extraneous pigmentation may be etiologically related. Of intrinsic pigmentation the most important are bile pigment and other derivatives of hemoglobin. Normally the liver cells usually show a varying number of fine yellowish-brown granules—some iron-containing (hemosiderin), some iron-free (hemofuscin); these are likely to be increased in atrophy of the liver cells from senility or other causes. Bile pigments (usually bilirubin, sometimes biliverdin) are found normally in the biliary passages; in cases of obstruction to the free flow of bile these pigments are found in excess in the biliary passages and also in the liver cells (particularly necrotic cells), and in the interstitial tissue. In malaria there occurs a deposit of fine dark-brown or brownish-black pigment granules, especially in the endothelial cells of the capillaries at the periphery of the lobules and in the perivascular connective tissue, and in Kupfer's star-like cells which act as phagocytes; occasionally there is some associated fibrosis that has been described as a malarial cirrhosis. A deposit of iron-containing pigment (siderosis of the liver) is found in and about various local lesions (abscesses, gummas, scars, tumors, etc.), in chronic passive congestion, cirrhosis, pernicious anemia, leukemia, and hemochromatosis; and a special metabolic pigmentation is found in melanotic sarcoma. Sprunt, Colwell and Hagan<sup>1</sup> believe that iron-containing, as well as other kinds of pigments, may be formed during autolytic degeneration of parenchymatous cells independently of the hemoglobin in the blood. In the nutmeg liver of chronic passive

<sup>1</sup> *Jour. Exper. Med.*, 1912, xvi, 607.



congestion, iron-free and iron-containing pigment is found in and about the central veins; it becomes quite conspicuous in the advanced stages (red atrophy), in which a large section of the central part of the lobules may show such pigmentation; later the iron reaction may no longer be obtainable. In pernicious anemia the periphery of the liver lobules usually contains a considerable excess of iron-containing pigment obviously derived from the hemoglobin of the erythrocytes; this is found also, but in less degree, in some cases of leukemia.

Special interest attaches to the process described as hemochromatosis, in which the liberated hemoglobin is deposited as pigment granules, in the skin, liver, pancreas, etc. Concurrently fibrosis of the liver and pancreas occur (pigmented cirrhosis with diabetes or bronzed diabetes).

**Leukemic Infiltration.**—The leukemic process commonly involves the liver: the lymphocytic variety always, the myelocytic variety almost always, although the disease may be quite advanced before noteworthy changes occur in the liver. The liver is enlarged, sometimes weighing 6000 grams or more, that is, three or four times its normal size; its surface is smooth, its edge somewhat rounded, and it is of lessened resistance and density. The section surface is smooth, pale, opaque, grayish, or sometimes yellowish in color. The individual lobules are usually distinguishable, and may appear to be more widely separated than normally (periportal leukocytic infiltration). Occasionally small roundish masses (lymphomatous masses), suggesting miliary tubercles, can be detected. Microscopically there is widespread leukocytic (lymphocytic or myelotic) infiltration; this is usually most marked in the periportal spaces where large masses separating the lobules are formed, but it involves also the lobules, being sometimes limited to the periphery, the capillaries of which may be fairly choked with leukocytes.

**Symptoms.**—The symptoms are those of leukemia, the enlargement of the liver being a part of the disease. The enlarged liver is painless, smooth, and has fairly sharp edges. Ascites, which is not rarely a terminal event in leukemia, has been variously interpreted. In many cases it is doubtless due to the blood dyscrasia and failing cardiovascular system, part of the generalized œdema or anasarca; perhaps in some cases it is due to peritonitis, sometimes tuberculous; but it has also been attributed to obstruction or thrombosis of the portal radicles.

The *diagnosis* is made by an examination of the blood. The *treatment* is that of leukemia.

**Necrosis.**—This may occur as a widespread or a limited process. The widespread process, such as occurs in thrombosis of the hepatic artery or the portal vein, in acute yellow atrophy of the liver, tropical abscess, etc., is elsewhere discussed. The limited process, so-called focal necrosis (Mallory<sup>1</sup>), occurs under a variety of circumstances and in several forms, which, however, are of pathological rather than clinical interest. Central, peripheral, and mid-zonal forms have been described;<sup>2</sup> the underlying factors of the varying zonal distribution of the necroses have not been definitely determined. Most of these necroses

<sup>1</sup> *Jour. Med. Research*, 1901, vi, 264; *Jour. Exper. Med.*, 1898, iii, 611.

<sup>2</sup> Opie, *Jour. Med. Research*, 1904, xii, 147.

are found in acute infections, such as typhoid fever, scarlet fever, diphtheria, pneumonia, cerebrospinal fever,<sup>1</sup> etc. In some cases, doubtless, they result from the direct action on the liver cells of bacterial toxins; in other cases they follow obstruction or occlusion of the capillaries by swollen, proliferated, or desquamated endothelial cells, transported giant (usually phagocytic) cells, fibrinoid plugs, thrombi made up of agglutinated erythrocytes, etc. Experimentally they may be induced by injection into lower animals of vegetable poisons, such as abrin and ricin (Flexner<sup>2</sup>), or of hemagglutinins of bacterial origin or those contained in certain cytolytic immune sera (Pearce<sup>3</sup>) which lead to the formation in the portal radicles of thrombi made up of agglutinated erythrocytes. These have a clinical interest in that they suggest the lesions as well as the mode of development of cirrhosis of the liver.

Oertel<sup>4</sup> has described a multiple non-inflammatory necrosis of the liver with jaundice, and he and Symmers<sup>5</sup> have carefully described the changes that occur in these necroses in the liver.

### ACUTE YELLOW ATROPHY OF THE LIVER

Acute yellow atrophy is an acute and widespread autolytic necrosis of the liver cells, characterized clinically by jaundice, reduction in the size of the liver, and toxic disturbances of cerebation, proceeding to a fatal issue. The disease is comparatively rare. The earliest record of a case is by Ballonius (died in 1616); Best,<sup>6</sup> in 1903, collected 450 cases. The best recent study is by F. W. White.<sup>7</sup>

**Etiology.**—Acute yellow atrophy is especially frequent between the twentieth and the thirtieth year (50 per cent. of the cases), and in women (two-thirds of the cases); both of these facts are explainable largely by the frequent occurrence of the disease during pregnancy. Hunter's studies show that more than 80 per cent. of the cases occur between the tenth and the fortieth year; Rolleston has collected 42 cases occurring within the first ten years of life. The influence of pregnancy is noteworthy, since almost if not quite half of the cases in women, that is about 30 per cent. of all cases, occur about the middle or during the latter half of pregnancy; the disease is scarcely if ever seen during the first three months of pregnancy, but sometimes it occurs during the puerperium. The onset of the disorder in pregnant women has been preceded by shock, fright, mental disturbances, worry, and anxiety (related or not to the pregnancy and expected parturition), all of which are believed to exert some influence; but it is extremely unlikely that these can do more than depress the general resistance. The causative

<sup>1</sup> Consult McCrae, *Jour. Path. and Bacteriol.*, Cambridge, 1908, xii, 279.

<sup>2</sup> *Johns Hopkins Hosp. Rep.*, 1897, vi, 259.

<sup>3</sup> *Jour. Med. Research*, 1904, xii, 329; 1906, xiv, 541. Pearce and Winne, *Am. Jour. Med. Sci.*, 1904, cxxviii, 669.

<sup>4</sup> *Jour. Med. Research*, 1904, xii, 75; *Jour. Exper. Med.*, 1906, viii, 103.

<sup>5</sup> *Jour. Exper. Med.*, 1907, ix, 64.

<sup>6</sup> *Thesis of the Univ. of Chicago*, 1903.

<sup>7</sup> *Boston Med. and Surg. Jour.*, 1908, clviii, 729 (literature).

influence of pregnancy is much more likely akin to that exerted by the toxemias of pregnancy, in which we now know the liver frequently shows degenerative changes, and in the production of which it plays an important, according to some observers the important, part. The actual etiological factor, however, is not known, since the disorder does not occur more commonly than once in 28,000 pregnancies (Braun). Various known infections exert some etiological influence; thus 10 per cent. of the cases occur during secondary syphilis (in which slight jaundice is not very rare). Various pyogenic infections (septicopyemia, osteomyelitis, etc.), typhoid fever, malaria, diphtheria, etc., have antedated the liver disorder. Microorganisms, especially the colon bacillus and pyococci, have been found in some cases, but being absent in most cases it is difficult to believe that they possess etiological significance; they are probably only secondary invaders. Etiological significance is also attributed to certain non-bacterial poisons, such as alcohol, chloroform, phosphorus, etc. Chloroform is of undoubted significance, being responsible for the cases of so-called delayed chloroform poisoning.<sup>1</sup> Opie<sup>2</sup> by the administration of chloroform accompanied by intravenous inoculation with *Bacillus coli* produced advanced hepatic cirrhosis accompanied by active new formation of bile ducts. Phosphorus gives rise to a somewhat analogous condition, but the lesions in the liver are not alike in the two disorders. Similar phenomena may develop in the course of other diseases of the liver, such as advanced passive congestion, cirrhosis, cholangitis, etc. All of the foregoing lead to the conclusion that the designation acute yellow atrophy, as well as icterus gravis, comprises a series of diverse disorders that exhibit more or less superficial resemblance. We are now able to separate some of the cases from the main group, such as those due to syphilis, septicopyemia, puerperal eclampsia, phosphorus poisoning, delayed chloroform poisoning, etc., but the definite etiological factor of the major group still eludes us.

**Pathology.**—The liver is much reduced in size and weight, being often one-half or one-third that of the normal (800 to 500 grams or less). The reduction is usually uniform, although occasionally more marked in the left lobe (possible site of beginning of the process); in other cases, there is more or less irregularity, due to varying grades of the destructive process or to attempts at compensatory hyperplasia. The organ is flaccid and has so lost its normal elasticity and resistance that it may be folded or bent upon itself; the capsule is wrinkled, obviously too large for the reduced organ, and if not thickened shows the liver to be greenish yellow, sometimes dirty dark grayish in color, with scattered areas more reddish or reddish brown in color; often small subserous foci of hemorrhage are also visible. On section the liver is found to be dense and resistant; the section surface is mottled—yellowish or yellowish-red areas of varying size and configuration alternating and more or less gradually merging the one into the other. The yellowish coloration is due chiefly, if not entirely, to bilirubin rather than to fatty alterations (the fat content is usually not increased, and may be diminished); the

<sup>1</sup> Consult Wells, *Arch. Int. Med.*, 1908, i, 589 (literature).

<sup>2</sup> *Jour. Exper. Med.*, 1910, xii, 367.



reddish areas seem to be an advanced stage of the yellow, and to be more numerous or larger the longer the patient lives.

Histologically the appearances vary with the stage of the disease. There is intense and widespread (not focal) destruction of the liver cells, which usually begins at the periphery and spreads to the centre of the lobules; early the cells are somewhat swollen and roundish in outline, but they soon become pale and granular, lose their outline, shrink, and stain poorly and diffusely, and the nuclei become obscured or dissolved. Usually they exhibit a yellowish color (staining with bilirubin). Ultimately the cells disappear, apparently in consequence of autolysis, and leave behind the supporting framework of the liver, granular debris, and endothelium of the capillaries (the reddish areas on macroscopic inspection). So extreme may be the destruction of the liver cells that the microscopic section can scarcely be recognized as liver tissue. Should the disorder be more or less protracted, a variable amount of new connective tissue is formed. In some specially protracted cases there are conspicuous evidences of attempts at regeneration (compensatory hyperplasia) of the liver cells.<sup>1</sup>

All the organs are more or less bile-stained. The spleen is soft, and is slightly or moderately, but not extremely, enlarged in about two-thirds of the cases. The kidneys are enlarged, softened, pale, opaque, and often reveal small foci of hemorrhage, cloudy swelling, and fatty changes. The heart also is swollen, softened, pale, and opaque (parenchymatous and fatty degeneration). The gastro-intestinal tract shows the lesions of catarrhal inflammation. Small hemorrhages are found beneath the skin and the various serous and mucous membranes, and are doubtless attributable to toxic changes in the blood and bloodvessels. Hemorrhages may occur also in the brain, and degenerative changes may be seen in the spinal cord. The blood itself is more fluid than normally, coagulates with difficulty, and readily stains the endothelium and adjacent tissues.

Studies of the chemistry of the liver by A. E. Taylor,<sup>2</sup> Wells,<sup>3</sup> and others show that not only is the fat content not increased, but that it may be actually diminished; this specially serves to distinguish the disorder from phosphorus poisoning, of which fatty changes constitute a conspicuous feature—30 per cent. as contrasted with 5 per cent. in acute yellow atrophy. In phosphorus poisoning the liver is enlarged, as a rule, whereas in acute yellow atrophy it is usually lessened in size.

**Pathogenesis.**—There are several conspicuous features of acute yellow atrophy that endow it with special characteristics: the rapid and marked reduction in size of a large solid organ, the speedy absorption of much of the necrotic cellular debris (in contrast with other forms of necrosis), and the appearance in the urine of leucin, tyrosin, and other amino-acids, products of destructive protein metabolism that do not occur in health. These seem unquestionably to point to the activity of some poison, virulent in nature and possessing a special affinity for the liver, upon

<sup>1</sup> Consult MacCallum, *Johns Hopkins Hosp. Rep.*, 1903, x, 375 (literature).

<sup>2</sup> *Jour. Med. Research*, Boston, 1902, iii, 424.

<sup>3</sup> *Jour. Exper. Med.*, New York, 1907, ix, 627.

which it acts widely and intensely. The source, nature, and exact mode of action of this poison are not definitely known. F. W. White supports the view, originally advanced by Flexner,<sup>1</sup> that the process is autolytic in nature, and that it is brought about by some poison having a specific action on the liver cells whose life it destroys without injuring the proteolytic ferments they contain, whence autodigestion ensues. The leucin and tyrosin result partly from autolysis of the liver, and partly from non-conversion into urea of leucin and tyrosin formed elsewhere. Other evidence of this autolysis is found in the albuminose and purin bodies (destruction of nuclein) sometimes encountered in the urine.

The jaundice is due to obstruction of the small biliary ducts by swollen and desquamated epithelial cells and by pressure from without exerted by swollen and necrotic liver cells; it is contributed to by destruction of erythrocytes and the formation of bile thrombi. The presence of bilirubin in the blood and the urine suggests that there is no suppression of the bile-forming function of the liver.

**Symptoms.**—The initial symptoms are those of gastro-intestinal catarrh, soon (one to four days) followed by jaundice; these may last a variable period, usually five to seven days, but sometimes several weeks. During this period the disorder is usually looked upon as ordinary catarrhal jaundice (cholangitis), and as a matter of fact there is little if anything to suggest the more serious disorder. The patient complains of malaise, perhaps fugitive neuromuscular pains, poor appetite, coated tongue, occasional vomiting, constipation, etc.; there is usually moderate jaundice and bile-pigment in the urine. Soon, however, the graver symptoms supervene. The jaundice deepens, becoming dark yellowish or bronze-like, slightly greenish (in rare, extremely rapid cases jaundice may be absent); severe nausea and vomiting set in and are often associated with hematemesis; diarrhœa may supervene; and grave nervous symptoms ensue—headache, photophobia, mental confusion, hebetude, and restlessness, soon followed by a noisy delirium, and later coma and perhaps convulsions. Hemorrhages (disordered nutrition of the vessel walls and hemolytic action of bile salts on the erythrocytes) occur beneath the skin and into and from divers mucous membranes (intestines, urinary tract, respiratory tract, genital tract, retina, and most commonly the stomach); absorption usually occurs in pregnant women. Soon the patient passes into a profound typhoid state. There may be slight fever (pyogenic infection?), but usually the temperature is below normal (until shortly before death, when there may be an agonal rise); the pulse becomes rapid, feeble, and of low tension; the respirations become accelerated and irregular; the pupils dilate (said to be important diagnostically); the tongue becomes dry, furred, and tremulous; sordes collect on the teeth and gums; and there are fibrillary twitchings.

The *liver* in some cases is found slightly or moderately enlarged in the early stages; this may be due to preëxisting disease (as cirrhosis), but rarely it seems to be a part of the acute yellow atrophy itself. Soon, however, the liver dulness diminishes rapidly in extent, until it may be

<sup>1</sup> *Amer. Jour. Med. Sci.*, 1903, cxxvi, 202.

entirely absent or constitute a small area in the axillary region; this is due to reduction in the size of the liver and to the fact that the small flabby liver falls away from the anterior abdominal wall and is replaced by the intestine. Death may occur before the liver lessens in size. The region of the liver may be tender on pressure. Slight or moderate enlargement of the *spleen* may be made out in about two-thirds of the cases; in the event of unusual hemorrhage or diarrhœa the spleen usually remains small.

The *urine*, as a rule, is lessened in amount, of increased specific gravity, of increased acidity, and highly colored (bile pigment and excess of urobilin); it usually contains a small amount of albumin, and hyaline, granular, fatty, and epithelial tube casts. The highly significant changes consist in the presence of leucin, tyrosin, and the other amino-acids (largely the result of autodigestion of the liver); sarcolactic, diacetic, and other fatty acids (lactic, acetic, butyric, and succinic); marked reduction in the amount of urea with an associated increase in the amount of ammonia and other nitrogenous substances. Sugar is rarely found. The amount of leucin and tyrosin is no index of the amount formed in the body (in the liver and elsewhere), since both substances are comparatively insoluble, and despite elimination, considerable of both substances may be found in the liver after death.

Examination of the blood often reveals a normal or an increased number of erythrocytes (usually attributed to concentration of the blood, although Grawitz and von Jaksch found the weight of the dried blood to be not above the normal); a moderate leukocytosis (up to 16,000) and a moderate reduction of the hemoglobin (60 to 80 per cent.). Bile pigments also may be found.

**Diagnosis.**—In the early stages there is scarcely anything to distinguish the cases from the more innocuous catarrhal jaundice, although jaundice and an enlarged and tender liver in a pregnant woman are of portentous significance. Careful studies of the urine, especially in pregnant women, and in cases of mild jaundice, and the detection of significant urinary changes, especially the evidences of an acid intoxication, should enable us to recognize the antecedent conditions and perhaps ward off the more serious later stages. The development of nervous symptoms in any case of jaundice should always awaken suspicion. When fully developed, jaundice, vomiting, delirium (and other cerebral symptoms), lessening in the size of the liver, and the presence of leucin and tyrosin in the urine are unmistakable. The presence of leucin and tyrosin is not unequivocal, since both substances may be found in small amounts in the urine in diseases in no way related to acute yellow atrophy, such as afebrile jaundice with slight enlargement of the liver, leukemia, erysipelas, typhoid fever, etc., and lessening in the size of the liver may be missed in those cases with cirrhosis (with a small liver), or when the liver is bound to the abdominal wall by adhesions.

*Phosphorus poisoning* may be excluded by the absence of a history of the ingestion of phosphorus (not always trustworthy), the latter development of jaundice (which in phosphorus poisoning usually supervenes after a day or two of symptoms referable to disordered stomach), decrease



in the size of the liver (which usually remains enlarged in phosphorus poisoning), the more severe nervous symptoms, and the constant occurrence and larger amounts of leucin and tyrosin. *Biliary cirrhosis* may be excluded by the presence of an enlarged liver with jaundice and fever, the absence of leucin and tyrosin from the urine, and the longer course.

**Prognosis.**—The disease runs a somewhat variable course. In a majority of the cases death ensues before the fourteenth day; almost half of the cases terminate fatally in from the fifth to the tenth day; a few cases become chronic and may last upward of four or six to eight weeks; rarely, but apparently undoubtedly, recovery may ensue, in which event the disorder is of much protracted course. Death before the fifth day is uncommon, except in pregnant women. The prognosis is extremely unfavorable, virtually fatal, the rare recovery serving rather to accentuate the ordinary course of the disease than to hold out hope of recovery in any particular case. The prognosis is especially bad in pregnant women, also in all cases, the more violent in nature and the earlier the onset of the nervous symptoms, in the event of serious renal complications, such as oliguria, albuminuria, casts, decrease in nitrogen excretion (evidences of toxic retention or acid intoxication), and in cases with severe hemorrhages. Virtually the prognosis depends upon the severity and length of the second stage of the disease; rarely this lasts more than two or at the most three days; should the symptoms be mild or abate, hope of ultimate recovery may be entertained, but usually the disorder becomes chronic and the patient eventually dies. The possibility of recovery, however, cannot be denied.

**Treatment.**—The extraordinary mortality shows the futility of therapeutic endeavors, nor can we hope for improvement until time and research have disclosed the cause. Perhaps it is too much to expect that we should view every case of jaundice as likely to eventuate in acute atrophy; but jaundice in a pregnant woman is assuredly serious, and should be looked upon as a possible forerunner of acute yellow atrophy. It is wise in all cases of jaundice in pregnant women (as well as in all cases of so-called catarrhal jaundice) to study the urine for evidences of acid intoxication and destructive protein metabolism, and, should these be found, to institute the appropriate treatment. Furthermore, in view of the similarity of the hepatic lesions in acute yellow atrophy, puerperal eclampsia, and delayed chloroform poisoning, chloroform and chloral should be used much more cautiously in pregnant women, especially in treating convulsions, than has been the custom.

In the early stages the patient should be confined to bed. Milk is the best food, and should be diluted with some alkaline mineral water; cereals and other carbohydrates may be given in considerable amounts, since they are likely to prevent or limit the acid intoxication. The bowels should be opened freely; calomel and the saline cathartics seem the best. Insistence should be laid upon the drinking of large amounts of water; any good water will suffice, but an alkaline mineral water is probably preferable. Alkaline diuretics may be added to the water or given otherwise, and should serve to promote the diuresis and counteract

the acid intoxication; sodium bicarbonate also might prove efficacious in the last-mentioned particular.

The guiding principles in the treatment of the second stage of the disease are similar to those of the first—to prevent or limit the formation and to promote the elimination of toxins. The measures mentioned should be continued, and free catharsis and free diuresis must be maintained; otherwise the treatment is purely symptomatic.

### CONGESTION OF THE LIVER

The liver, being a large organ well endowed with bloodvessels, and interposed between the portal circulation and a large area of the systemic venous circulation opening almost directly into the heart, is naturally responsive to variations in the inflow of portal blood on the one hand, and the outflow of the general systemic venous blood on the other hand; to these must also be added its responsiveness, in common with other organs of the body, to the supply of arterial blood. The amount of blood contained within the liver, therefore, is subject to wide variations in health, and it varies also in disease with the factors upon which it is dependent. That the liver is capable of accommodating an extraordinary amount of blood is obvious from the great size it often attains when congested, and the very marked reduction in size that may follow relief of the factors provoking the congestion (such as gastro-intestinal hemorrhage, improvement in chronic heart disease, etc.). The increased amount of blood may be due to increased inflow or impeded outflow of the blood—whence we may distinguish an active and a passive congestion, but neither can be looked upon as a disease entity. The one is largely toxic in nature and usually gastro-intestinal in origin; the other is largely mechanical in nature and usually cardiac in origin.

**Active Congestion.—Etiology.**—This may result from an excess of blood from the portal vein or the hepatic artery; the portal vein is the more important factor. This active congestion develops under a variety of circumstances: (1) It occurs as a physiological process during digestion, when the amount of blood carried to the liver by the portal vein is increased, lessening and finally subsiding as digestion proceeds to its completion. (2) Various poisons, some endogenous, some exogenous, may be carried to the liver by the portal vein and provoke acute congestion. (3) Active congestion of the liver may also result from the action of the toxins of certain infections that may reach the liver by way of the general circulation, such as malaria, pyococcic infections, typhoid fever, yellow fever, influenza, etc. In some of these infections the poison may reach the liver by way of the portal and the general circulation. (4) There is a group of cases presumably of active congestion of the liver attributed by men of experience to the influence of “cold.”

It is obvious that many of the aforementioned factors are the causes also of inflammation and of degenerative changes in the liver, and, as a matter of fact, it is difficult in many cases to separate the one condition from the other; indeed, in some cases they are combined. Degenerative

changes are very common in all toxemias, and are not uncommonly associated with congestion; and congestion itself is an early stage of inflammatory conditions. In many cases the changes represent gradations of the one process, which, depending upon the severity and virulence of the operating cause, in the one case ceases at congestion and subsides, and in the other progresses to inflammation.

**Pathology.**—The liver presents the ordinary appearances of active congestion (which, however, after death are ill marked); it is enlarged, swollen, and contains an increased amount of blood, whence it is somewhat dark reddish or reddish brown in color, and it drips blood on section. Microscopically there is dilatation of the capillaries and small vessels of the capsule of Glisson; often there is parenchymatous and sometimes fatty degeneration, occasionally pigmentation of the liver cells. Rarely there is oedema, congestion, and proliferation of the biliary ducts.

**Symptoms.**—These are rarely unequivocal. Most of the cases follow or are associated with dietetic indiscretions, and the symptoms are largely those of disturbances of digestion, which in general partake of the complex popularly designated “biliousness.” In consequence of an excess of food or too much alcohol, excessive demands are made upon the liver; the wheels of catabolism become clogged and the drains of excretion more or less plugged; the blood becomes surcharged with partially detoxified protein substances and effete material, and a “bilious,” “lithemic,” or “gouty” attack supervenes. The appetite is poor, temporarily lost, the sight or thought of food often exciting disgust; there is a bad taste in the mouth and the tongue is furred; there is epigastric distress, which sometimes amounts to actual pain and is usually aggravated by taking food; nausea is common and vomiting may supervene; there is often discomfort and sometimes actual pain in the region of the liver, which rarely is referred to the right shoulder and scapula, increased by deep breathing, sudden movement, and lying on the side; usually there is constipation and the stools may be light colored, but there may be transitory attack of diarrhoea. The patient’s general feelings are often distressing; there is general malaise, headache, sometimes vertigo, a feeling of nervousness with unrefreshing sleep, irritability, depression, etc. Occasionally there is slight jaundice; more often there is a peculiar sallowness of the face and the general integument. The liver is found enlarged and tender, but the enlargement is not marked. The urine is commonly concentrated, of increased specific gravity, and deposits an abundant sediment of urates and uric acid; occasionally there is a transitory (toxic) albuminuria. Bile pigments are present in the event of jaundice. The disorder is usually afebrile, although now and then there may be a rise in temperature to 100° F. or thereabouts (in which event the disorder should be viewed as having progressed to acute parenchymatous hepatitis).

In another class of cases, those met with in infections, such as dysentery, etc., the constitutional symptoms are the more marked, slight or moderate fever is usually present (progression to acute hepatitis), and the local gastro-intestinal symptoms are more or less in abeyance, but become aggravated during digestion. The liver is enlarged and tender.



**Diagnosis.**—This is usually apparent from the etiological factors, the general disturbances of the gastro-intestinal tract, the slight jaundice, and enlargement and tenderness of the liver; by no means of minor diagnostic importance is recurrence of attacks in a person of known ill-chosen habits of eating and drinking. The difficulties consist in determining whether or not to the congestion permanent damage to the liver tissue has been added. With recurrence of attacks, their increasing duration, and lessening intervals, this becomes the more likely; the less the enlargement of the liver and the quicker it subsides (or returns to the normal), the more is permanent damage unlikely. In the more acute cases encountered in infections aggravation of the constitutional symptoms, together with enlargement and tenderness of the liver, usually suffice for diagnosis. In these cases there are usually parenchymatous changes in addition to the congestion.

**Prognosis.**—The disorder rarely lasts more than three or four days; sometimes a week. It is not dangerous in itself, but acquires its importance because of its etiological factors (especially alcohol) and its frequent recurrence in those who persist in the use of alcohol, in whom it is likely to eventuate in cirrhosis, and in those continuously exposed to other etiological factors, such as dysentery, etc., in the tropics.

**Treatment.**—There is reason to believe that in those who eat and drink too much and lead a sedentary life, in the gouty, those of plethoric habit, and those formerly the subjects of chronic malaria, dysentery, etc., in the tropics, prophylactic measures may serve to ward off attacks, at least recurrences, of acute congestion of the liver; and it is by no means unlikely that appropriate energetic treatment undertaken early in cases of what cannot be called other than acute congestion would often prevent the later development of cirrhosis. Obviously those factors known to provoke an attack of acute congestion should be avoided, and one should cultivate abstemious habits. The food should be moderate in amount and easily digested; highly seasoned articles should be avoided; alcohol should be omitted altogether or taken only occasionally, as whisky in small amounts, well diluted, and with the meals. The body, especially the abdomen and back of the neck, should be protected from the action of "cold" by day as well as by night. Constipation should be overcome, preferably by laxative foods, an occasional mercurial purge, and the saline cathartics. The too common sedentary life should be at least partially replaced by activity.

When the attack has developed the patient should go to bed and be kept there until convalescence is complete. The guiding principle should be to reduce the functional demands upon the liver, to eliminate all factors that might provoke or add to its congestion, and to reduce any existing intestinal catarrh. These objects are best achieved by dietary regulations. The diet should be minimal in amount and absolutely unirritating; in general it should consist exclusively of milk, which should be given at stated (rather long) intervals, and well diluted with lime-water or other alkaline water. Whey, junket, albumin water, strained broths (without seasoning), barley water, calf's-foot jelly, etc., may be given later, and, indeed, early to those who seriously

object to or are inconvenienced by milk. Gradually the diet may be augmented, at first by the addition of cereals, and then meat, etc. Alcohol must be absolutely interdicted. Plain or alkaline water should be given in large amounts throughout. The congestion of the liver and the intestinal catarrh are influenced by free saline purgation.

Ammonium chloride (20 grains thrice daily) has long enjoyed a reputation in the relief of disorders of the liver. It may be given in the early stages, combined with the alkalis (alkaline waters, sodium bicarbonate, etc.), or later with nitrohydrochloric acid, nux vomica, or strychnine, and a bitter tonic. The distressing gastric irritability of the early stage of some cases may be controlled by sodium bicarbonate, bismuth subnitrate, and carbolic acid or creosote. Local measures, such as leeches, cold compresses, etc., sometimes relieve the local discomfort, and are believed by some observers to lessen the congestion of the liver.

Those subject to recurrences of congestion of the liver are much benefited by treatment at some of the well-known spas, such as Carlsbad, Marienbad, Vichy, etc. Many of the waters of our own country, such as Saratoga, etc., are equally efficacious, but there is little if any control of the patient at the resorts, and the accessories are largely wanting.

**Passive Congestion.—Etiology.**—This is due to factors that impede the efferent circulation; these are largely mechanical in nature and cardiac in origin (whence the name cardiac liver). The disorder occurs: (1) In failure of the heart, whether acute or chronic; it is most common as well as most advanced in the late stages of mitral valve disease (especially mitral stenosis) with consecutive tricuspid insufficiency; but it is found also in primary tricuspid disease, in advanced aortic valve disease (with secondary mitral and tricuspid disorder), myocardial weakening with dilatation, pericardial adhesions, etc. (2) It occurs also in the advanced stages of such diseases of the lungs as cause increased work of the right side of the heart and ultimately lead to its failure, such as emphysema, chronic bronchitis, asthma, chronic adhesive pleuritis, and compression of the lungs (by pleural exudates, mediastinal tumors, aneurisms, etc). (3) It may result also from local factors that obstruct the circulation about the junction of the hepatic veins and the inferior vena cava, of which the most important are kyphosis and scoliosis, tumors, hydatid cysts, gummas, etc., of the liver, inflammatory bands and adhesions, and kinking of the hepatic veins or the inferior vena cava by a displaced heart or a large pleural or peritoneal effusion.

**Pathology.**—Passively congested livers may be divided into three classes, more or less distinct, but representing different stages of the same process: (1) The merely congested or engorged liver, found in cases of acute or recent heart failure (common in the infections, such as pneumonia, typhoid fever, etc.), and in chronic valvular disease with well-maintained compensation in which death has occurred suddenly or after a few days' illness only; (2) the congested nutmeg liver, found in cases of long-standing heart disease with dilatation of the right heart and tricuspid insufficiency, in which compensation, although precariously maintained, has been on the whole fairly satisfactory, and in which no

serious or prolonged failure has occurred until that which leads to death; and (3) the fibrotic nutmeg liver, found also in cases of long-standing heart disease with dilatation of the right heart and tricuspid insufficiency, in which one or more severe and prolonged attacks of failure of compensation have occurred, during which the auricle has suffered especially and, being perhaps totally incapacitated, has permitted the full force of the ventricle to be transmitted to the hepatic lobules with consequent rupture of the venules and capillaries, laceration and destruction of hepatic parenchyma, and its repair by new-grown connective tissue.

The congested liver in the early stages is increased in size, depending upon the amount of contained blood: it is firmer and denser, and dark purplish or bluish in color. On section the liver in the early stages drips blood and presents a more or less uniformly congested dark bluish or purplish color, sometimes slightly mottled with lighter areas; in more advanced stages the excess of blood is less apparent, and the organ presents the characteristics spoken of as the congested nutmeg liver; the intralobular and sublobular venules being distended and overfilled with blood, appear as dark purplish or reddish spots (transverse section) or streaks (longitudinal section), which are in marked contrast to the pale yellowish or whitish circumferential liver cells, the seat of fatty infiltration and biliary pigmentation. When of still longer duration, the liver has decreased in size and may be less than normal; it is firmer and denser, but still presents the nutmeg appearance; about the distended central veins some fine new connective tissue, often pigmented, reddish in color, may be obvious; the hepatic veins are dilated and their walls thickened and opaque; the adjacent hepatic tissue is atrophic and pigmented, and invading it fine fibrous connective-tissue trabeculae may be detected (fibrotic nutmeg liver; red atrophy of the liver). The capsule is sometimes thickened and opaque, especially in the event of ascites, and through it the distended subcapsular veins may be apparent. In some cases there may be a more or less universal perihepatitis, commonly associated with pericarditis and pleuritis (so-called multiple serositis). More or less extensive hemorrhage into the centre of the lobules and consequent destruction of the hepatic parenchyma are not uncommon. The hepatic cells about the central veins show a variable degree of atrophy—partly a pressure atrophy and partly doubtless nutritional, the result of insufficient oxidation or due to toxins or cytolytic ferments. In most cases there is a considerable accumulation of fat in the liver cells; usually, also, the cells about the central venules contain more or less pigment derived from the hemoglobin, usually hematin, but also hemosiderin. In consequence of atrophy of the liver cells the supporting reticulum becomes relatively increased, and it becomes absolutely increased in consequence of new growth (replacement fibrosis). This fibrosis is usually most marked about the central vein, and it gradually radiates therefrom, following the capillaries throughout more or less of the lobule. There is always more or less fibrosis about the hepatic veins, which, as a rule, is proportionate to the degree and duration of the congestion. About the portal veins also some fibrosis may now and then be observed, but this is always minor in grade and altogether



disproportionate to the fibrosis observed elsewhere. The capsule is usually thickened, and from this new connective-tissue trabeculae usually invade the liver a variable distance to join the new perilobular connective tissue.

The new-growth of fibrous tissue has led to its comparison with cirrhosis, and the term *cardiac cirrhosis* has been employed. But the lesions are in no way comparable to those of ordinary cirrhosis. The slight fibrosis common in the congested nutmeg liver is intimately related to the central and sublobular and hepatic veins; it results no doubt from the chronic distension of the veins; but the more marked fibrosis in the fibrotic nutmeg liver is doubtless in large part a replacement or scarring process, to repair destroyed liver parenchyma. Such periportal fibrosis as occasionally occurs is purely subsidiary, and may readily be accounted for by the fact that hepatic vein obstruction may lead to portal congestion, which in turn sets up chronic intestinal catarrh; the poisons thus induced may be transported by the portal vein to the liver and induce a mild grade of portal cirrhosis; in many cases of chronic heart disease, alcoholism is quite common, and may set up an ordinary cirrhosis; and finally, many cases of ordinary portal cirrhosis have added passive congestion. The phenomena should be correctly interpreted; the liver in passive congestion rarely presents the lesions of true cirrhosis.

Much interest attaches to the proper interpretation of the aforementioned lesions. Of special interest is the idea advanced by Salaman<sup>1</sup> that the liver acts physiologically as a safety valve to the heart, and that the various changes in structure undergone after prolonged back-pressure modify that safety-valve action and seriously alter the clinical course of the disease. Salaman states that the structure of the liver may be aptly compared to that of a sponge, and that in consequence of the elasticity of the supporting framework as well as of the parenchyma, the organ is capable of considerable expansion with subsequent recovery of shape, hastened by the pressure of the other abdominal organs.

The congestion of the liver in the early stages of cardiac failure is a compensatory process; this is especially active in acute failure, such as occurs in many infections and in the early stage of chronic valvular disease; not until the liver has been distended to and beyond its capacity does œdema ensue; and with the progress of the valvular defect and the gradual loss of the safety-valve action of the liver (due to the described lesions), œdema appears more and more easily.

**Symptoms.**—These consist of (1) those due to the primary cardiac or pulmonary disease; and (2) those due more directly to the disorder of the liver itself, which consist of local distress and gastro-intestinal phenomena. The severity of the local subjective symptoms often depends more upon the rapidity of the development of the congestion than upon its grade; that is, subjective symptoms may be for some time in abeyance if the congestion develops slowly, although it may reach a high grade; whereas a less grade of congestion, developing rapidly, may occasion considerable distress. In one class the manifestations of cardiac failure predominate; in another class, phenomena referable to the liver predominate.

<sup>1</sup> *Lancet*, Lond., 1907, i, 4.

Chief among the local symptoms are pain, superficial and deep tenderness, and distress or a sense of weight and heaviness in the right hypochondrium, aggravated by pressure, motion, deep inspiration, and the lateral posture. The congestion in the hepatic veins leads to congestion also in the portal tributaries, with consequent disturbances in digestion, poor appetite, epigastric distress, especially after eating, flatulence, nausea, constipation, etc. *Jaundice* is a common phenomenon; usually it is slight or moderate in grade, in which even the admixture of cyanosis and jaundice lends a very characteristic bluish-green or greenish-blue discoloration. The jaundice may be due to compression of the biliary capillaries and consequent interference with the flow of bile; perhaps more commonly to radicular cholangitis; or to the extension of the intestinal catarrh to the diverticulum of Vater and the common bile duct, in which event the obstruction is rarely complete; that is, some bile appears in the stools. In rare instances a terminal infection leads to marked increase of the jaundice (sometimes associated with mental symptoms, *icterus gravis*), doubtless due to toxic destruction of the hepatic cells. Oedema and ascites are common.<sup>1</sup> The oedema is usually preceded for some time by enlargement of the liver, except in cases in which there is a sudden and severe cardiac collapse. One is warranted in the assumption that oedema does not supervene until the liver has exerted to the utmost its safety-valve action, and that the readiness with which oedema appears and disappears is a tolerably accurate indication of the functional activity of the liver in this respect. The ascites may be part of a general dropsy and due solely to the factors provoking the anasarca, in which event it is likely to be small in amount, proportionate to the oedema; or it may be disproportionate, large in amount, and require frequent tapplings; in this event it is associated with the fibrotic congested liver, or with chronic adhesive peritonitis (perihepatitis) or a more generalized peritonitis. An acute peritonitis may supervene, with audible and palpable friction.

Examination of the liver reveals it to be enlarged; the size varies from time to time, depending upon the condition of the heart. The organ may be palpable a full handbreadth below the costal margin; it is uniformly smooth, has a sharp or slightly rounded edge, and is usually more or less tender. In advanced stages the liver becomes reduced in size (reduction in the amount of blood, cicatrization of connective tissue, atrophy of parenchyma), and may even recede beyond the costal arch, so as no longer to be palpable. The enlarged liver not infrequently pulsates. The pulsation being usually systolic in time and truly expansile is more likely to be found in early stages, before new-grown fibrous tissue interferes with expansion of the organ. True pulsation must be distinguished from a non-expansile pulsation transmitted to the liver by the contracting hypertrophied heart, by an abdominal aneurism, etc. Polygraphic tracings are really necessary often to detect pulsation and to properly time it. Mackenzie<sup>2</sup> believes that once the liver has begun to pulsate, it continues to do so until death. If the pulsation is

<sup>1</sup> Pitt, Allbutt and Rolleston, *System of Medicine*, 1909, vi, 325.

<sup>2</sup> A Study of the Pulse, 1902, Edin. and London.

synchronous with the contraction of the auricle, Mackenzie has shown that stenosis of the tricuspid valve will frequently be found. The enlarged liver causes proportionate displacement and compression of adjacent organs; it may cause collapse of the base of the right lung, with dulness on percussion and feeble or absent breath sounds (which should not be mistaken for pleural effusion).

The urine is concentrated, of high specific gravity and high color; it contains an excess of urobilin, and usually a small amount of albumin. The albuminuria is proportionate to the cardiac debility, and disappears with improvement in the cardiovascular condition.

**Diagnosis.**—This is usually evident from a knowledge of the primary disorder, an enlarged and tender liver, and other evidences of failing cardiac compensation. The enlarged and congested liver may usually be readily distinguished by the fact that its volume changes considerably from time to time, which does not obtain in the case of other enlarged livers, and that lessening in the size of the liver is commonly associated with other evidences of improved cardiac tone and an increase in the amount of urine. Congestion may be distinguished from *cirrhosis* of the liver by evidence of the primary cardiac or pulmonary disorder, other evidences of failing heart, a smooth liver, the absence of dilated abdominal veins, and by the response to medication directed to the condition of the heart; but one must remember that congestion is not uncommon in *cirrhosis* of the liver, and that the marked reduction in the size of *cirrhotic* livers is often due to lessening of congestion rather than to atrophy of hepatic parenchyma. The smooth surface and varying size of the liver, responding to treatment directed to the heart, and the absence of cachexia will usually serve to exclude malignant disease; absence of the etiological factors will usually exclude amyloid disease; and an examination of the blood will exclude leukemia.

**Prognosis.**—This depends altogether upon the primary disorder, upon the outlook and the response to treatment of the provoking cardiac disorder. To some extent, especially in acute and sudden failure of the heart, the congestion of the liver is doubtless a compensatory and more or less beneficent process. In chronic and advanced cases of heart disease this function becomes gradually abolished and the outlook correspondingly bad. Only the fibrotic nutmeg liver can be said of itself to influence materially the prognosis, which, from the very nature of the process, it renders very gloomy, presaging the fatal termination.

**Treatment.**—The treatment is that of the primary cardiac or pulmonary disorder causative of the hepatic congestion; virtually, whatever the primary disease, the treatment is that of failing cardiac compensation. The patient must be absolutely at rest so as to reduce the work of the heart. The diet should be light and nutritious; fluids should be small in amount. Digitalis is the sovereign remedy, but it may seem desirable to supplement its action by such other drugs as *strophanthus*, caffeine, camphor, etc. The Addison, or Guy pill, consisting of digitalis, squill, and mercury (calomel or blue-mass), is valuable in many cases. Diuretics, such as theobromine, the potassium salts, etc., may also be given with hope of benefit. Bleeding is often efficacious.



The hepatic congestion is also favorably influenced by cathartics, especially the saline cathartics, the natural aperient waters, etc., which should be given in quantity sufficient to cause free watery movements. The vegetable cathartics also are useful, especially in connection with a relatively dry diet, for several days, from time to time. Pain in the region of the liver may be relieved by hot compresses, an ice-bag, etc. General nervousness and insomnia are often markedly benefited by morphine hypodermically:  $\frac{1}{32}$  to  $\frac{1}{16}$  grain usually suffices and is quite as efficacious as, if not more so, than larger doses. Bromides, chloralamide, trional, veronal, and other hypnotics may be tried from time to time. Œdema may require punctures and the use of Southey's tubes, and ascites may require repeated tapings. The tapping should not be too long delayed if the patient suffers much distress; on the other hand, it should not be performed too rapidly, nor too much fluid withdrawn, since the removal of the pressure sometimes permits the rapid absorption of toxic substances and leads to the speedy development of uremic manifestations.

### PERIHEPATITIS

**Acute Perihepatitis.**—**Etiology.**—This is almost, if not quite, without exception a secondary disorder. Rarely it follows trauma of the right side (contusions, fractures of the ribs, etc., with or without contusion or laceration of the liver and its capsule); in the great majority of cases the perihepatitis is secondary to disease of the liver or adjacent viscera. It occurs in association with acute congestion and inflammation of the liver (especially in the tropics); it is not uncommon in long-standing passive congestion; it occurs in various forms of suppuration within the liver; it is associated with tubercles, gummas, and rapidly growing new growths of the liver that reach to or project beyond the surface; it follows inflammatory and ulcerative processes in adjacent organs, such as ulcers of the stomach, duodenum, and other parts of the intestine, cholecystitis, pancreatitis, appendicitis, etc., in which circumstance the lesions ultimately often are those of one form of subphrenic abscess; it may be part of a general peritonitis; and it may follow disease of the thoracic viscera (pleuritis, pericarditis, etc.) through extension through the diaphragm. Acute perihepatitis is obviously always the result of infection; the common infecting agents are the pyogenic cocci (staphylococci and streptococci), the pneumococcus, the colon bacillus, etc.

**Pathology.**—The lesions may be localized or diffuse, and fibrinous, serofibrinous, or purulent in character. Early the peritoneum loses its lustre and becomes dull and opaque, the vessels become injected, and a small amount of serum or serofibrin is thrown out. The lesions may not extend beyond this: the serum becomes absorbed and the fibrinous exudation undergoes organization, with the ultimate formation of filamentous or dense adhesions. The lesions vary in situation with that of the primary cause: in traumatic cases, and those associated with various diseases of the liver itself (abscess, gummas, new growths, etc.),

and of the thoracic organs, the lesions are most likely to be on the antero-superior surface of the liver, and the ultimate adhesions bind the liver to the diaphragm and the anterior abdominal wall; in the cases that follow disease of the adjacent abdominal organs the lesions are most likely to be at the contiguous, usually inferior, surface of the liver; in cases due to transport of infection from a distance (appendicitis for instance) the lesions are most common on the superior aspect of the organ; but most unlooked-for lesions sometimes occur. In other cases the lesions progress to suppuration.

**Symptoms.**—The important clinical phenomena consist of local pain and audible and palpable friction, which are quite similar to the analogous pleuritis. The pain is often acute and lancinating; it may be located anywhere in the region of the liver, but it is not infrequently referred to the margin of the ribs and the epigastrium (fairly widespread perihepatitis), or rather high up in the axilla (more localized peritonitis), and it frequently radiates to the supraclavicular fossa (said by Cantlie to be diagnostic); it is made worse by motion, such as deep inspiration, or the lateral posture, or by passive motion made by the physician. The movements of the right lower chest are restricted or abolished. Palpation reveals local tenderness and not infrequently rigidity of the upper abdominal muscles on the right side. Auscultation may reveal friction which, however, is often quite localized and very fleeting; rarely it may be palpated. Sometimes there is slight or moderate fever; there may be a short, hacking, dry cough sometimes set up by manipulations of the liver. Hiccough (suggesting involvement of the diaphragm) is not uncommon and may be severe. Nausea and vomiting may occur in case the stomach, duodenum, or gall-bladder are implicated in the inflammation. Occasionally slight ascites develops—due to interference with drainage of the peritoneum through the diaphragm; this is quite independent of the marked ascites due to general peritonitis, etc.

**Diagnosis.**—This is not infrequently obscured by the predominance of symptoms of the primary disorder; sometimes the lesions are found after death in cases in which no noteworthy symptoms were present during life. However, the diagnosis can usually be made by noting the symptoms of the primary disorder, and in addition local pain and tenderness, audible and sometimes palpable friction, and perhaps rigidity of the abdominal muscles of the right upper quadrant. The condition is probably most commonly mistaken for right-sided pleurisy—which may coexist; the acute perihepatitis, however, can usually be distinguished by a knowledge of the primary (usually abdominal) disorder, the lower situation of the local signs, and the onset of severe pain upon passively moving the liver forward and backward (Cantlie).

**Prognosis.**—This depends upon the primary or underlying condition; the acute perihepatitis (unless it progresses to suppuration), although distressing, is not in itself dangerous to life.

**Treatment.**—The treatment is that of the primary disease; but in some cases the phenomena of the acute perihepatitis so overshadow those of the primary disease as to furnish the indications for treatment. Pain often demands immediate attention and may be relieved by

strapping the side; this may obviate the necessity of giving opium, which should not be withheld should the pain continue. In some cases more or less relief attends the use of poultices, an ice-bag, dry cupping, leeches, and other forms of counterirritation, etc. The patient should be kept at rest and on a light diet until the acute manifestations have subsided, whereupon the treatment should revert to that of the primary disorder.

**Local Chronic Perihepatitis.—Etiology.**—This not infrequently follows acute perihepatitis, particularly repeated attacks, and it is due, therefore, to the same causes. It is perhaps most commonly found in association with chronic passive congestion of the liver (long-continued expansion and contraction of the liver with consequent peripheral friction), pressure atrophy (corset liver, etc.), gummatous and tuberculous new formations, tumors and hydatid cysts reaching the surface of the liver, chronic cholecystitis, gastric and duodenal ulcers, etc.

**Pathology.**—In many cases local chronic perihepatitis represents the process of healing of acute perihepatitis by the formation of adhesions, in which event the process is obsolete, non-progressive; the adhesions are firm, fibrous, and non-vascular; they are attached to, and virtually form a part of, the capsule of the liver; and they serve to bind the liver to adjacent structures and tissues—the diaphragm, the gall-bladder, the anterior abdominal wall, the stomach, duodenum, pancreas, intestine, omentum, etc. In some cases adhesions have not formed, the capsule of the liver revealing here and there more or less localized thickenings, much resembling the so-called milk spots of the pericardium. Rarely there appears to be some progression from the local to the general form of perihepatitis, but, as a rule, the two are quite distinct.

**Symptoms.**—These are scarcely, if ever, definite; but local pain, tenderness, and rigidity, particularly if recurrent, may suggest the disorder; confirmation may rarely be obtained by eliciting audible or palpable friction. In some cases the diagnosis may become apparent by the onset of an acute exacerbation. In the majority of cases the diagnosis is not likely to be made—which is a matter of little or no moment, since the disorder is of comparatively little clinical importance.

**Treatment.**—This is altogether that of the primary disorder. In rare instances in which the chronic perihepatitis can be diagnosed, and the still rarer instances in which special treatment seems indicated, the measures mentioned in acute perihepatitis are appropriate.

**General Chronic Perihepatitis; Chronic Hyperplastic, Hyaline, or Deforming Perihepatitis; Sugar-iced Liver (Zuckergussleber); Multiple Serositis; Polyorrhymenitis; Pericarditic Pseudocirrhosis of the Liver (Pick).**—This is a disorder first described by Van Deen, later studied by Curschmann, who gave to it the name of Zuckergussleber (sugar-iced liver), and more recently studied by Hale White, Nichols, Rolleston, etc.<sup>1</sup>

**Etiology.**—General chronic perihepatitis is about equally common in the two sexes; it occurs at all ages, but is most common in the second

<sup>1</sup> A review of the literature, with a collection of cases and some personal observations, will be found in *Multiple Serositis*, by A. O. J. Kelly, *Amer. Jour. Med. Sci.*, 1903, cxxv, 116.



and the fifth decades. The exciting causes are ill understood; most likely they are toxic in nature, but the nature and source of the toxin are not known. The rather common association of the condition with arteriosclerosis and chronic interstitial nephritis (19 of Hale White's 22 cases) suggests that the poison may be allied to that of uremia, but this supposition is somewhat negated by the rarity of chronic perihepatitis in arteriosclerosis and chronic nephritis. It is not improbable that the arteriosclerosis, nephritis, and perihepatitis may be due to the one cause, unknown as it may be. That the etiological factor is often widespread is shown by the common association of disease of several serous membranes (peritoneum, pericardium, and pleura). The process is best explained upon the assumption of a bacterial toxin that finds in the peritoneum (or other serous membrane), reduced in vitality from any cause (such, for instance, as nephritis), a favorable soil for activity. In some cases this poison may be that of malaria, typhoid fever, or other infections; in other cases it may be syphilitic, although syphilis usually causes only a local perihepatitis; in other cases it is undoubtedly tuberculous, although the lesions are not those ordinarily provoked by the tubercle bacillus; but in many apparently non-tuberculous cases characteristic tuberculous lesions may be detected and the tubercle bacillus may be recovered from the lesions. McWeeney<sup>1</sup> suggests that the bovine tubercle bacillus may be the cause in some cases. In most cases, however, no definite etiological factor can be determined.

**Pathology.**—At first sight the cases appear to be separable into two classes, those in which the lesions are confined to the peritoneal investment of the liver, and those in which they involve also the serous membranes above the diaphragm (pericardium and pleura); but that this is an artificial division is obvious from the fact that the perihepatitis is often only part of a more generalized chronic peritonitis, and that the ultimate lesions are identical, whether they begin below or above the diaphragm; the condition essentially is a chronic multiple serositis.

The lesions consist of the development of a thick encasement of fibrous connective tissue, whitish, glistening, and much resembling confectioner's icing, whence the name iced-liver or sugar-iced liver (*Zuckergussleber*). This encasement may envelop the liver completely, or be limited to, or most marked upon, the upper surface; it may be 5 mm. or more in thickness; it is often of cartilaginous consistency; and it can usually be detached in layers, leaving what appears to be a more or less intact peritoneum (this is quite characteristic, and serves to distinguish this from other forms of perihepatitis). This new connective tissue exhibits a marked disposition to cicatricial contraction, so that considerable distortion of the liver ensues, the narrower anterior margin in particular being frequently distorted. The gall-bladder is commonly embedded in dense adhesions and may be discovered and isolated only with great difficulty; usually it is collapsed and contains little or no bile, perhaps a small amount of mucus. The lesions not uncommonly involve the pleura (especially the right), and the pericardium, but also other

<sup>1</sup> *Trans. Roy. Acad. Med., Ireland*, Dublin, 1906, xxiv, 402.

abdominal viscera; the spleen may be similarly encased in a thick, whitish envelope; the omentum may become thickened, indurated and rolled upon itself, forming a hard, almost unrecognizable mass; the mesentery may become thickened and much shortened, in consequence of which the intestine also becomes shortened and perhaps obstructed. In many cases the most widespread adhesions and distortion of the abdominal organs ensue, giving rise to what has been aptly described as deforming peritonitis. Of 110 cases collected by Picchini (50 observed by himself and 60 collected from the literature), the peritoneum was involved in all (although this was recognized clinically in only 13), being, therefore, the most frequent and most important lesion; pleuritis was present in 109 cases, in 73 of which it was bilateral; the pericardium was involved in 9 of 50 cases.

In 39 cases collected by Kelly, with special reference to the association of chronic obliterative pericarditis and ascites, the pericardium was obliterated in all (more or less extensively calcified in 10); the right pleura was entirely obliterated in 17, and was partially obliterated or contained fluid in 19 (in 3 the condition of the right pleura was not stated); the pleura was entirely obliterated in 15, it was partially obliterated or contained fluid in 16, it was normal in 3 (in 5 the condition of the left pleura was not stated); in 28 cases there was chronic perihepatitis, and in 31 cases chronic peribepatitis or chronic peritonitis, or both.

The condition of the *liver* is of much interest. In many cases, aside from distortion and compression, there are no noteworthy lesions—a fact of much importance in determining the pathogenesis of the lesions. In the 39 cases mentioned, the liver was reported as nutmeg in 14, cirrhotic in 8, normal aside from compression in 4, nutmeg and cirrhotic in 4, and in 3 there appeared to be only extension of connective tissue from the thickened capsule into the substance of the organ. In these cases (Pick's pericarditic pseudocirrhosis of the liver) the nutmeg appearance of the liver may well be attributed to a failing heart; these do not include the many in which the pericardium is not involved, and in which congestive changes in the liver are rare, unless there be a failure of the myocardium from other causes. In these cases, although a slight amount of fibrosis may extend from the thickened capsule a short distance into the substance of the liver, cirrhosis in an acceptable sense does not occur; but one must remember that thickening and adhesions of the capsule are not uncommon in advanced cirrhosis. The *spleen*, in addition to being incased in a thick connective-tissue envelope and adherent to adjacent structures, especially in association with left-side pleuritis, is not infrequently enlarged, especially in the cases associated with chronic pericarditis (23 of the 39 cases already referred to). The kidneys usually exhibit the lesions of chronic interstitial nephritis, more so perhaps in the cases in which the lesions are confined to the peritoneum.

Microscopically the encasing is seen to consist of new-grown fibrous connective tissue, for the most part arranged in lamellæ, and the seat of advanced hyaline degeneration (whence Nichols speaks of the condition as hyaloseritis); there are very few bloodvessels, and a small amount of round-cell infiltration—leukocytes and mast cells. Usually

there is a more or less sharp line of demarcation between the new tissue and the underlying capsule of the liver.

As already stated the lesions may begin in any one serous membrane, and then remain localized thereto or gradually spread to the others. De Renzi believes that the peritoneum is usually involved first; then the right pleura, and then the pericardium. If, however, the right pleura should be involved first, the disease then extends to the peritoneum, thence to the left pleura and the pericardium. In some cases this mode of progression of the disease is not preserved, as sometimes a pericarditis, usually not to be diagnosed, develops first. The intensity of the lesions about the liver finds its explanation in the normal circulation in the peritoneal cavity, whereby fluids and foreign particles, regardless of the position of the patient, are carried toward the upper surface of the liver; the lymphatics converge toward the suspensory ligament of the liver and the central tendon of the diaphragm. The attempt on the part of the peritoneum to remove certain noxious agents may result in partial or complete success. In the latter instance the peritoneum may be completely rid of the infective agent, which being carried to the mediastinal lymph vessels and glands, may infect the pericardium or the pleura, giving rise to a primary pleuritis or pericarditis; subsequently the peritoneum, by a descending infection, may become involved. In other cases the attempt on the part of the peritoneum to remove the infective agent being only partially successful, the region about the liver and the under surface of the diaphragm succumbs, and a primary perihepatitis occurs. Subsequently the infective agent may travel through the diaphragm and infect the pericardium or the pleura, or both. The peculiarities of course and of distribution of the lymphatics of this region are also accountable for the much greater involvement of the upper surface of the liver, as contrasted with the lower surface, that is present in most cases. De Renzi states that the disease is characterized by the fact that it remains localized to the serous membranes; that it does not implicate the intra-abdominal and intrathoracic organs; that it pursues a remarkably slow and insidious course; that it gives rise to the exudation of large quantities of serofibrinous fluid; and that the fluid portion of the exudate tends to become absorbed, in consequence of which adhesions with obliteration of the serous cavities result.

**Symptoms.**—The disorder often remains latent for many years, and may be entirely unsuspected during life; in other cases there is often a more or less clear history of the past occurrence of inflammation of one or more serous membranes; and in still other cases it is only examination of the patient that discloses the serous membrane disorder. In the cases with manifest symptoms, the most common are sensations of fulness, oppression, and weight in the upper abdomen; or there may be apparently a sudden onset with acute pain. The abdomen increases in size and may attain very large dimensions—due to ascites. With increase in the amount of ascites, the abdominal wall becomes tense and the other subjective symptoms aggravated. There may be slight and transitory jaundice. Later, œdema of the legs may develop.

A striking feature is the *ascites*, which is present whether the



pericardial and pleural changes are absent, slight, or marked. Aside from ascites, the clinical picture varies somewhat, depending upon the seat of origin of the disease. In some cases the disease is ushered in with acute pericarditis, pleuritis, or perihepatitis, which subsides and leaves the patient apparently well for a number of years. Usually, however the lesions of the pericardium and of the pleura are latent, and the first sensible evidence of the disease is ascites. In some cases of primary pericarditis, slight and transient œdema of the legs may be present early, but this is not observed in many cases, inasmuch as the pericarditis is usually latent. When œdema is present early it usually soon subsides and does not recur until the ascites has been present for a long time or until shortly before death; except shortly before death it is inconspicuous when contrasted with the excessive ascites. Associated with early œdema, slight swelling of the spleen and disturbances of the gastro-intestinal tract may develop, but these usually subside with the œdema, and the disease, as a rule, is characterized by the entire absence of such symptoms, until failure of the heart supervenes, or until shortly before death. The ascites is characterized by the fact that it is excessive, that it necessitates repeated tapplings, that it recurs rapidly after tapping, and that it may remain stationary (not requiring tapping) for many years. Osler mentions a child in whom tapping was done 121 times, and Rumpf mentions a case in which tapping was done 301 times. The ascitic fluid is amber in color, has a specific gravity above 1.015, as a rule, and contains upward of 3 per cent. of albumin—which suggests its inflammatory nature. After repeated tapplings, it may be impossible to draw off much fluid on account of the presence of many adhesions. The liver may or may not be palpable (depending upon the presence and the grade of congestion); it is usually not palpable in the late stages. The indurated and rolled up omentum may be palpable as a transverse mass; it should not be mistaken for the lower border of the liver. The general condition remains for a long time but little disturbed. The gastro-intestinal functions, as a rule, are well performed, and emaciation is long postponed. In some patients the urine may reveal the usual changes of chronic interstitial nephritis, or those of passive congestion. In other cases there are the obvious symptoms and signs of arteriosclerosis. Finally, in most cases the heart fails or death may be due to some intercurrent complication, such as pneumonia.

**Diagnosis.**—Recurrent ascites in a person in otherwise good health, together with the disposition and ability to be up and about between tapplings, should suggest the diagnosis. Of special diagnostic significance are a history of a previous attack of pericarditis, pleuritis or perihepatitis; the early occurrence and subsequent disappearance of œdema of the legs; marked ascites with little or no œdema of the legs; an enlarged liver early (this may not occur), and a small and distorted but otherwise smooth liver late in the course of the disease; the absence or very late occurrence of marked enlargement of the spleen; a tendency to the repeated occurrence of attacks of pain, tenderness, rigidity, and possibly palpable and audible friction in the right hypochondriac region—attributable to the attacks of perihepatitis; and the rapid recurrence of ascites

after tapping. One should always endeavor to determine whether the lesions are confined to the region about the liver or are more widespread, involving the pericardium and the pleura. In these cases one must endeavor to dissociate the symptoms due to the serositis from those due to failure of the circulation induced by the pericardial part of the serositis and its consequences. In most of these cases prime importance attaches to the recognition of an adherent pericardium.

From *cirrhosis* of the liver the condition may be distinguished by the signs of adherent pericardium; the absence of the etiological factors of cirrhosis of the liver; the slow, insidious, protracted, and intermittent course; the long periods during which the ascites may remain stationary and the patient in good condition; the entire absence or transient presence of slight jaundice; the absence, in most cases, of portal congestion and gastro-intestinal disturbances; in some cases, the association of an enlarged, smooth, and firm liver with marked ascites; and the fact that in many cases the patient survives a large number of tapplings. Syphilis may be suggested by the history of past infection and the other evidences of syphilis; but gummas may be present in the liver and be associated with perihepatitis and ascites without other evidences of the infection. The diagnosis sometimes can only be made by resort to the Wassermann reaction or the therapeutic test. The ordinary *tuberculous peritonitis* is suggested by less exudation, other tuberculous foci in the body, perhaps induration about the umbilicus, and the presence of fever. *Malignant disease* of the liver is suggested by irregular, nodular enlargement of the liver, evidence perhaps of primary tumor formation elsewhere in the body, and a more rapid course.

**Prognosis.**—This is bad as to eventual recovery, but the patient may live for many years. In more than 70 per cent. of the cases the duration is two years or more; in more than 50 per cent., four years or more; and it may be as long as sixteen years. The general health and strength are maintained for a long time, and the patient may go about his business between tapplings. Sooner or later the periods between tapplings become less, cardiac failure supervenes, or death results from some infection.

**Treatment.**—This is almost wholly symptomatic, for little can be done to influence the progress. Diuretics may effect the discharge of the too abundant fluid or a similar object may be achieved by free catharsis. Potassium iodide and mercury or salvarsan may be tried when there is a trustworthy history of syphilis, as well as in doubtful cases, since they hold out some hope of benefit. Tapping must be performed when necessary; usually it has to be done frequently, and although occasionally the fluid remains at a standstill for long periods of time, tapping usually has to be resorted to at gradually decreasing intervals. Permanent drainage subjects the patients to the danger of infection and acute peritonitis. Operative interference, such as the Drummond-Talma operation, is theoretically contra-indicated, and practically has not been attended by any benefit in the few cases in which it has been tried.

### ACUTE HEPATITIS

The phenomena to which the term acute hepatitis are applicable may be divided into the suppurative and the non-suppurative forms, both of which conform to rather definite clinical and pathological types. The suppurative form comprises the different forms of abscess, suppurative pyelephlebitis, suppurative hepatic phlebitis, suppurative cholangitis, etc. The non-suppurative form comprises a series of most diverse disorders that exhibit all stages of progression, from active congestion to the inflammatory focal necroses of many infections (localized process) and the more widespread process manifested clinically as the different forms of icterus gravis and acute yellow atrophy of the liver.

**Acute Non-suppurative Hepatitis.—Etiology.**—This may result from the factors that provoke active congestion and parenchymatous degeneration. The most common causes are the toxins of different infectious diseases, exogenous poisons, such as alcohol and phosphorus, and certain endogenous autotoxins possibly of gastro-intestinal origin, etc. The lesions vary with the virulence of the toxic cause, the duration or recurrence of its activity, and the resistance of the liver cells. As a matter of fact, acute hepatitis is uncommon in temperate climates, the different bacterial toxins rarely producing changes surpassing parenchymatous degeneration or cloudy swelling, unless we view as inflammatory the different forms of focal necrosis common in infections that sometimes are surrounded by inflammatory zones. Alcohol, especially if taken in fairly large amounts, undiluted, and at rather frequent intervals, induces, as a rule, only an active congestion, sometimes also more or less parenchymatous degeneration (and leads ultimately to cirrhosis).

In the tropics a disorder described by those of experience as acute parenchymatous hepatitis (tropical liver) is of frequent occurrence; it is most commonly provoked by malaria, but also by dysentery and kala-azar and perhaps other infections. It occurs especially in young adult Europeans, and not uncommonly soon (during the first year) after their arrival in the tropics. Undoubtedly factors other than malaria and dysentery are active, although these may be the exciting causes acting upon a liver reduced in vitality. The influence of immoderate eating (especially of animal food), of drinking (especially alcohol), of exposure to cold and fatigue, may not be overlooked.

**Pathology.**—The lesions are most diverse, and no one description could accurately include the manifold variations, combinations of congestion, cloudy swelling, focal necroses, and the vascular and other phenomena of inflammation. The lesions vary from small focal necroses, small opaque areas, scarcely obvious to the unaided eye, to the more complete or universal involvement of the organ. In slight or moderate cases the appearances of the liver are those of active congestion and cloudy swelling; in the more severe cases they vary in grade up to those of acute yellow atrophy. In general one may say that the liver is enlarged, swollen, softened, and rather pale in color; the section surface also is pale and opaque, and not infrequently mottled. Microscopically, in addition to swelling, increased granulation and opacity of the liver cells,



and obscuration of their nuclei, dilatation of the capillaries, arterioles, and venules, one encounters also fatty degeneration and pigmentation of the liver cells, thrombosis of certain capillaries and other small vessels, focal necroses, more or less round-cell infiltration, swelling and desquamation of the endothelium of capillaries, and swelling, œdema, proliferation, and desquamation of the cells of the small biliary ducts. In some (protracted) cases, looked upon by many authors as a subacute form of acute yellow atrophy, there is more or less compensatory hyperplasia of the liver cells. In most cases, other parenchymatous organs, especially the kidneys and the heart, exhibit similar changes.

**Symptoms.**—The symptoms virtually are those of active congestion, of which acute hepatitis is only an advanced stage. Perhaps, although not necessarily, the symptoms are more aggravated in the inflammatory than in the merely congestive disorder; the liver pain and tenderness are likely to be more marked; nausea and vomiting are more common and usually more severe; the vomited matter partakes of the so-called bilious character (greenish, watery), and not infrequently contains blood—due usually to violent and distressing retching that provokes marked thirst and ultimately may induce marked prostration or collapse; the bowels are likely to be constipated, but the constipation may alternate with a foul, ill-smelling diarrhœa; and the nervous symptoms, such as headache, restless irritability, depression, etc., are usually more marked. Jaundice is scarcely more common or more marked than in active congestion; usually it does not amount to more than a subicteric tint to the conjunctiva or a peculiar sallowness of the general integument. The *liver* is enlarged; sometimes, especially in early cases, notably so, when it may reach as low as the umbilicus; it may also be markedly increased upward, perhaps irregularly so; it is not likely to exhibit much enlargement in advanced cases (due doubtless to the presence of new-grown connective tissue—developing cirrhosis). The spleen is enlarged in the cases due to malaria, but usually of normal size or only slightly enlarged in other cases. The urine, as a rule, is concentrated, high-colored, of increased specific gravity, and deposits an abundant sediment of urates and uric acid; occasionally there is a transitory (toxic) albuminuria. Bile pigment is present in the event of jaundice. That, however, which distinguishes the inflammatory from the congestive disorder is the presence of fever. It is true that slight fever, less than 100°, sometimes attends what is looked upon as congestion merely; but the gradual progression of the one disorder to the other is obvious, not only in the etiological factors and the general symptomatology, but also in the occurrence of fever. A temperature of 100° or more may be looked upon as conclusive evidence of the inflammatory nature of the disorder.

In the class of cases difficult to classify, but which exhibit various clinical and pathological relations and graduations to certain types of icterus gravis, the onset of the disorder is sometimes sudden and may be attended by a chill or chilliness and soon followed by fever; vomiting may set in, and may be succeeded by diarrhœa; slight (toxic or hemolytic) jaundice is rather common; the liver becomes enlarged, sometimes irregularly so; and the constitutional symptoms are usually severe.

**Diagnosis.**—This is usually apparent from the etiological factors and the general symptoms, as narrated. The difficulties are in excluding other disorders, such as the different forms of suppurative hepatitis, and in the presence of jaundice, the different forms of toxic jaundice and acute yellow atrophy. In the early stages it may and frequently is quite impossible to differentiate between suppurative and non-suppurative hepatitis; in some cases time alone gives the diagnosis. In some cases the one is a later stage of the other, and the suppuration may not be susceptible of recognition until the development of the general phenomena of the condition—irregular chills, fever, sweats, etc. In acute yellow atrophy the constitutional and nervous symptoms are more severe, the liver, at first enlarged, becomes small, the duration is less, and the outcome usually death. Phosphorus poisoning is suggested by the etiology, the enlarged liver, gastro-intestinal hemorrhages, severe constitutional and nervous symptoms, etc.

**Prognosis.**—The first attack of acute non-suppurative hepatitis, especially as observed in the tropics, usually lasts about a week or ten days, and results in recovery; in some cases, however, suppuration ensues. One attack predisposes to subsequent attacks, and with each recurrence the course and termination are less favorable; the liver may remain more or less enlarged and gradually become cirrhotic, or, as in some primary attacks, the process may go on to suppuration.

**Treatment.**—The prophylaxis and treatment are as in active congestion of the liver. In addition, in those cases due to malaria, quinine should be administered in good doses; its use is often followed by a notable and rapid diminution in the size of the liver. In the event of recurring attacks the patient should remove from the tropics to a more temperate or cooler climate. Much benefit may be obtained by a course of treatment at some one of the well-known spas, Carlsbad, Marienbad, etc.

**Suppurative Hepatitis.**—Suppurative hepatitis, or abscess of the liver, occurs under a variety of circumstances and in several forms. There is some justification for the common division into two classes—the large, single, so-called tropical abscess, and the small, multiple, non-tropical abscesses; but the processes are not altogether different, since the tropical abscess may be double instead of single, and even when single, by infecting adjacent liver tissue may give rise to the development of many secondary abscesses, and a number of small abscesses by peripheral extension may coalesce and give rise to a large single abscess. It seems wise, therefore, to discuss suppurative hepatitis as a single process.

**Etiology.**—Abscess of the liver is always the consequence of infection; the agents are various, and reach the liver by one of several pathways. The common causative organisms are the ordinary staphylococci and streptococci, *Amæba coli* (*Entamæba histolytica*), *Bacillus coli communis*, *Bacillus pyogenes fetidus*, *Bacillus typhosus*, *Bacillus dysenteriae*, *Bacillus pyocyaneus*, *Diplococcus pneumoniae*, *Proteus vulgaris*, *Actinomyces bovis*, etc. The infecting agent or agents may reach the liver directly, as when in consequence (1) of traumatism bacteria are introduced directly into the liver, or (2) when they reach the liver by extension of disease of adjacent organs; or the infection may be carried from afar by the blood-

stream, that is, (3) by the portal vein, (4) by the hepatic artery, (5) by the hepatic veins, (6) by the biliary ducts, or (7) by the lymphatics. The abscesses that result from traumatism or the extension of disease of adjacent organs are sometimes spoken of as primary, whereas those that result from the transport of infection from distant parts are called secondary abscesses; this distinction, however, is of little or no practical importance and cannot always be maintained.

1. *Traumatism* occasionally gives rise to abscess of the liver. The resulting abscess is usually single and small or moderate in size.

2. *Diseases of adjacent organs* rarely give rise to abscess of the liver, but occasionally an ulcerative or suppurative (usually calculous) cholecystitis may perforate into the adjacent hepatic tissue and set up suppuration; or after the formation of adhesions, a gastric or duodenal ulcer or an ulcerating gastric carcinoma may invade the liver tissue and induce suppuration therein. The abscess is usually single and small, but sometimes it attains considerable size.

3. *Infection by way of the portal vein* is the commonest cause. In the great majority of cases dysentery, especially amœbic dysentery, is an antecedent condition, and the resulting abscess in the liver is spoken of as the single, tropical, or amœbic abscess. This form, whether or not it is accompanied by pyelphlebitis, is characterized usually by the development of small multiple abscesses; occasionally, however, a single large abscess is produced, or it results later from the coalescence of several smaller abscesses.

The most common cause of this form of liver suppuration in temperate climates is *appendicitis*. In this the portal vein and its branches may or may not reveal thrombophlebitis, and the infection of the liver may result from extension of the thrombophlebitis, from metastases by way of the portal vein from the local disease in and about the appendix (the most common mode), or from transit of the infection through the retrocecal tissues to the liver. Other gastro-intestinal disorders also occasionally engender abscess of the liver, such as gastric and duodenal ulcers (transport of infection by the portal vein in the absence of adhesions), pyococcic, typhoid, tuberculous, actinomycotic, and neoplastic ulcers of the small and large intestine and the rectum, suppurative lesions of the pelvic organs (male and female), hemorrhoids, and infected thrombi following operations upon the intestine, rectum, anus, etc.

A solitary abscess of the liver may be a *hydatid cyst*, in which secondary infection has occurred.

4. *Infection by way of the hepatic artery* is rather uncommon and gives rise to small multiple so-called septicopyemic abscesses. These occur in pyococcic infections, especially infective endocarditis, purulent and fetid bronchitis, bronchiectasis, abscess and gangrene of the lungs, purulent pleuritis, suppurative periostitis, suppurative otitis media, infected operative or non-operative wounds, etc.

5. *Infection by way of the hepatic veins* may occur under exceptional circumstances, in which emboli may drop from the superior vena cava through the right auricle into the inferior vena cava and the hepatic veins. Perhaps it occurs also in other cases in which pyogenic bacteria



from a suppurative focus in the pelvis or lower extremities, coming up the ascending vena cava, are forced into the hepatic veins by some violent motion and by a retrograde process infect the liver. This is most likely to occur with myocardial weakness and venous congestion.

6. *Infection by way of the biliary ducts* gives rise to abscess formation in the liver and in one of three ways: (1) By direct transport of the infection by way of the biliary passages themselves, such as may occur in infectious or suppurative cholangitis and pericholangitis, with extension to the adjacent interlobular tissues and the formation of multiple small abscesses; (2) by the extension of the infection in the biliary passages through the biliary mucosa to the subjacent vessels, thence to the portal vein (into which they empty), and the production of suppurative pylephlebitis, in which event the process is analogous to that described in connection with infection by way of the portal vein; and (3) by direct extension of ulcerative and suppurative processes in the biliary tract (usually calculous cholecystitis) to the adjacent liver tissue.

7. *Infection by way of the lymphatics* may cause abscess of the liver under circumstances analogous to those that occasion infection by way of the portal circulation. In some cases, doubtless, the portal vein becomes involved after the infection has first gained the regional lymphatics; in other cases in which liver abscess, especially suprahepatic abscess, follows peritoneal disorders, the infection has followed the pathway of the lymphatics which converge from the peritoneum to the upper surface of the liver; in some cases of amœbic abscess of the liver the amœbæ probably reach the liver by traversing the peritoneum.

**Pathology.**—Abscesses the result of traumatism and of ulcerative and suppurative processes in adjacent organs are usually single and small or moderate in size, although those due to disease of adjacent organs sometimes attain considerable, usually superficial, extent. Inasmuch as these abscesses usually are situated near and involve some one of the surfaces of the liver, there is commonly a more or less extensive perihepatitis, adhesions binding the liver to the diaphragm or the adjacent organs. In some cases the collection of pus is on rather than within the liver, and merits the designation suprahepatic or infrahepatic abscess. In the small multiple metastatic abscesses that are not uncommon in general arterial pyemia (hepatic artery infection) or portal pyemia (portal vein pyemia), and sometimes occur in retrograde emboli (hepatic vein infection), or follow suppurative cholangitis, the liver is usually enlarged, swollen, and opaque, and presents the ordinary evidences of parenchymatous degeneration or cloudy swelling.

**Symptoms.**—Attempts are sometimes made to distinguish acute, subacute, and chronic abscesses; the distinction, however, is quite artificial, since although acute, subacute, and chronic abscesses do occur, a chronic abscess may remain latent for a long time and reveal itself acutely in consequence of some accidental disorder, such as trauma, intercurrent disease, etc., and suppuration that began acutely may subside and become virtually a chronic abscess. The symptoms of suppurative hepatitis vary with the nature and seat of the antecedent disorder, the pathway of infection, and the nature and virulence of the infectious

agent. Many cases, especially of so-called tropical abscess, are entirely latent; often they are not detected until they have lasted some time; not uncommonly they constitute an unexpected finding at the necropsy.

*Traumatic abscess* as well as abscess due to spread of disease from adjacent structures, usually manifests itself by pain in the region of the liver, aggravated by motion and pressure, and referred to the right shoulder; palpable and audible friction (attributable to local perihepatitis); perhaps jaundice due to compression of the biliary ducts; chills, fever, sweats, and leukocytosis; enlargement of the liver, usually irregular; and perhaps a fluctuating tumor. The sequence of these phenomena upon an obvious trauma, especially if the skin and subcutaneous tissues have been lacerated, gives to them peculiar diagnostic significance that can scarcely be misinterpreted; to these are sometimes added the discharge of pus through the wound, whereupon one has only to decide whether the abscess is about or involves the liver tissue. The detection of hepatic cells in the pus or in scrapings from the base of the abscess cavity settles the diagnosis, which, however, is usually a matter of academic interest, since the treatment cannot be other than surgical.

*Multiple septicopyemic abscesses*, whether due to portal vein, hepatic artery, hepatic vein, or biliary duct infection, often are not diagnosed; in perhaps the majority of cases their existence can be suspected only; that is, the symptoms of the primary disorder overshadow those due to the infection of the liver. In the one case the symptoms are those of a primary suppurative process in the heart (ulcerative endocarditis, purulent pericarditis), in another case in the lungs (abscess of lung or empyema); again, in the abdominal or pelvic viscera or in the extremities. The primary local process may be more or less obvious, and the general symptoms, chills, fever, sweats, and leukocytosis, are usually referred thereto; pain in the region of the liver may be inconspicuous or misinterpreted; the liver may not be noticeably enlarged (since death usually ensues early); pain in the shoulder may be interpreted as due to arthritis. In many cases the diagnosis of the liver involvement is of academic rather than of practical importance, since the condition is one of general septicopyemia, of which the hepatic involvement may be only a minor part; and its detection would not notably influence either the diagnosis or the treatment, although it might add materially to the seriousness of the prognosis. In some cases, however, particularly of so-called portal pyemia, but also of general arterial pyemia, or of spread of infection to the liver from suppurative cholangitis, the diagnosis is possible from a knowledge of the primary disorder and the development of local symptoms referable to the liver, the onset of which may be manifest by an aggravation of the general symptoms, especially the fever, sweating, and leukocytosis (or the marked decrease of a previous well-marked leukocytosis, significant of lessening general resistance). The significant local symptoms consist of pain in the region of the liver referred to the right shoulder, tenderness about the liver, perhaps a mild grade of jaundice, and enlargement of the liver. The enlargement may be quite regular, but the organ is likely to be softer rather than

harder than normal; sometimes the enlargement is irregular and nodular, and the nodules may be soft or semifluctuating; in this event audible or palpable friction (perihepatitis) may be detected.

The so-called *tropical abscesses* and other liver abscesses of *intestinal origin* and slow (or comparatively slow) development are, as a rule, much more readily diagnosed; but some are so indefinite in their manifestations as to escape detection. Generally the onset is slow and insidious; sometimes for weeks or months the patient may complain of general ill-health; malaise, or gradually increasing weakness—which are especially significant if they constitute part of the poor health or delayed convalescence from dysentery and other intestinal disorders attended by suppuration or ulceration (such as appendicitis, etc.). In some cases the onset is sudden, attended by a chill or chilliness, and follows directly upon these intestinal diseases; in other cases, although the noteworthy symptoms develop acutely, the antecedent disorder was present at some more or less remote time, and the abscess, doubtless previously latent, has been awakened into activity by some accidental cause. In another series of cases there have been one or several, sometimes recurring, attacks of what one may interpret as acute congestion of the liver, or acute hepatitis, especially in the tropics.

Suppuration of the liver is sometimes first suggested by *pain*, but one must remember that even a very large abscess may be altogether unattended by pain. In some cases early in the disease the pain is like that already mentioned in connection with active congestion or acute non-suppurative inflammation of the liver (due to tension of the capsule), which in reality usually precede the abscess formation. Pain when present varies with the situation of the abscess; when situated deep within the liver there may be no pain whatever, since the liver parenchyma is insensible to pain; the nearer the surface and the more marked the involvement of the liver capsule the more marked the pain; it may be acute, or merely a sense of weight or discomfort that may be increased by motion. With the progress of the abscess formation deep within the liver substance, the initial pain, that due to tension on the liver capsule, may entirely disappear (often occasioning an unwarranted sense of satisfaction); and it reappears when the abscess has reached the surface and provoked a perihepatitis, in which event the pain may be quite like that of pleuritis. The pain is not infrequently referred to the right shoulder, especially below the acromion process of the scapula, where it is usually dull and aching; this is said to be most common when the abscess is in the right lobe of the liver (the great majority of cases); occasionally it is referred to the left shoulder (abscess in the left lobe, in some cases at least); rarely it is bilateral. This pain also is due to the perihepatitis, which irritates the phrenic nerve which communicates with the superficial cervical plexus; the pain, therefore, is not significant of suppuration as such.

*Jaundice* is present in about 16 per cent. of the cases (58 of 375 cases, Thierfelder); usually it is slight, rarely marked. It is due to pressure of the abscess on adjacent biliary ducts or to intrahepatic cholangitis.



*Constitutional* symptoms, especially chills, fever, and sweating, significant of suppuration under all circumstances, are of importance. A chill is not uncommon at the onset of the suppuration, and a chill or chilliness, especially toward evening with a rise in the temperature, is rather frequent; but in some cases that develop slowly and become well encapsulated a chill may be missed—entirely or until late in the course. Fever is an extremely important symptom, and probably essential to the diagnosis. It varies much in different cases. In perhaps the majority the elevation is in the evening; but the fever may be more or less continuous (especially early in the disease), remittent, or intermittent; sometimes the diurnal fluctuations are quite marked—96° to 104° or 105° F. In chronic and well-encapsulated cases the fever range may be slight; sometimes there is apparently no fever at all or only slight and transitory attacks; rarely the temperature is subnormal. Sweating is a common, almost a constant symptom; it is usually most marked at night, but may occur irregularly during the day, especially if the patient sleeps. Often the sweats are very profuse, and give rise to great debility. The skin in many cases is frequently moist and clammy, especially upon the slightest exertion. Other manifestations of the general toxemia are seen in arthritic pains, and sometimes swelling of the joints (toxic synovitis and arthritis), and in certain nervous symptoms, such as headache, nervousness, insomnia, irritability, depression, etc.

Examination often discloses a general and facial aspect, the hepatic facies, readily recognized and of much diagnostic significance. The patient obviously is sick; the facial aspect is one of anxiety, distress, and more or less suffering; the complexion is muddy or sallow, or slightly icteric; the general integument is now hot and dry, now cold and moist; loss of flesh is progressive and is more marked the more severe and the longer the duration of the disease.

The *liver* is usually enlarged, although in some cases when the abscess is deeply seated and small, and sometimes even when it is quite large, no very noteworthy enlargement may be detected. The situation and direction of the enlargement depend upon the situation and direction of the abscess; since this is usually in the right lobe, the enlargement is usually in the right hypochondrium. In the early stages, when the abscess is still within the substance of the liver the enlargement is usually tolerably uniform; but as the abscess increases in size it commonly causes disproportionate enlargement of the liver upward and a corresponding change in the hepatic dulness; this often assumes a characteristic dome shape; that is, the upper limit of hepatic dulness rises near the mammillary line, reaches its highest point near the midaxillary line (where it may be on a level with the fourth or the third rib), and then descends, so that in the midscapular line it may be as low as the angle of the scapula. A decline of the upper limit of hepatic dulness near the vertebræ is quite characteristic of liver abscess. In some cases these changes are not present, as when the abscess occupies the left lobe, or when the enlargement of the liver is lateral rather than upwardly, or downwardly and anteriorly; in the last mentioned event there may be bulging beneath the margin of the ribs or in the epigastrium, where on

palpation one may detect a rounded or globular, smooth, and tense or semifluctuating tumor (depending upon whether the abscess actually projects beyond the surface or is still within the substance of the liver). In some cases definite fluctuation may be elicited. When enlargement cannot be made out by the usual methods, recourse may be had to the x-rays, which will readily disclose any irregular enlargement as well as the usual limitation of the movement of the diaphragm.

As the abscess approaches or reaches the surface of the liver perihepatitis is set up and friction may be detected; this suggests the point of election in the event of resorting to exploratory puncture. The muscles of the right upper quadrant of the abdomen become tense and unyielding, and there is usually considerable local tenderness. In some cases also there is local œdema, confined to one or two intercostal spaces or involving almost if not quite all the surface projection of the liver.

The urine is concentrated, of high color, increased specific gravity, and deposits an abundant sediment of urates and uric acid; as a rule, the amount of urea is diminished, but this is quite variable, although it is likely to be lessened if there is much destruction of the liver tissue; indican, a small amount of albumin and albumose are sometimes present. Examination of the blood may reveal leukocytosis—a total count of 25,000 or more—and a relative increase of the polynuclear neutrophiles; unfortunately leukocytosis is not always found; it is likely to be absent in slow-growing, chronic, and well-encapsulated abscesses.

There are a number of other signs and symptoms that occur in varying combinations in different cases and are due to variable conditions. Thus, certain gastro-intestinal symptoms may develop, such as nausea and vomiting, which are most common when the left lobe is involved (local adhesions or pressure on the pylorus or duodenum); the appetite is usually poor, and the tongue coated in the centre, or smooth, red, and fissured; there may be constipation (usually when the abscess is latent) or diarrhœa (when there is marked congestion of the liver or the acute hepatitis of the tropics); sometimes an obsolete dysentery is reactivated; and large amounts of pus may appear in the stools if the abscess ruptures into the bowel. *Amœbæ* may be found in the stools, especially if there is diarrhœa; when there is constipation they may be found in the mucus that often coats the feces. The growth of the abscess upward, together with restricted movement of the base of the right chest and of the diaphragm, cause more or less congestion and compression of the base of the right lung, and lead to cough, dyspnœa, impaired percussion resonance, feeble or bronchovesicular breath sounds, and fine râles; later, pneumonia may develop. In some cases a short, hacking, spasmodic cough ensues; it is usually referable to irritation of the diaphragm or an actual pleuritis, which in turn may have been due to transport of infection through the diaphragm or to rupture of the liver abscess into the pleura. The cardiac action may be embarrassed by the pressure of a large abscess, and the pulse rapid and irregular. The spleen usually is not enlarged and not palpable. Ascites does not occur unless there is some causative complication.

Spontaneous *rupture* is a common event in the course of large, especially tropical, abscesses of the liver. In Cyr's<sup>1</sup> series of 563 cases, rupture occurred in 159 (28.2 per cent.), as follows: Into the lung in 59, the pleura in 31, the pericardium in 1, the peritoneum in 39, the intestines in 13, the stomach in 8, the kidney in 2, etc. In Thierfelder's<sup>2</sup> collection of 170 cases perforation occurred into the lung in 74, the pleura in 26, the pericardium in 4, the intestines in 32, the peritoneum in 23, the stomach in 13, the kidney in 1, etc.

In a majority of the cases rupture occurs upward through the diaphragm (57 per cent. of Cyr's cases, 59 per cent. of Thierfelder's cases). In some cases purulent pleuritis results and gives rise to the usual signs thereof; in other cases (hepatopulmonary abscess) the pus finds its way into the lung either directly, in consequence of the early formation of adhesions (which is the rule), or indirectly, following a purulent pleuritis. When rupture occurs into the lung and the process finally involves and perforates a bronchus, a large amount of pus (perhaps mixed with blood) may be suddenly coughed up, or it may come up with very little effort, being evidently discharged in consequence of the release of the tension of the abscess; so great may be the amount of pus thus released that the patient's lungs may be inundated and sudden death may ensue. In other cases smaller amounts of pus are coughed up from time to time, but the total amount in the twenty-four hours may be considerable—ten to twelve ounces or more. The expectorated pus may exhibit ordinary purulent characteristics and contain necrotic liver tissue; usually, however, in the early stages at least, there is more or less blood mixed with the pus. Amœbæ may be found in it, should they be the exciting cause. Should the condition progress favorably, which it does in many cases, the amount of pus expectorated gradually diminishes and ultimately ceases, and the patient recovers. In other cases the expectoration lessens or ceases, but the patient's general condition becomes worse, and chills, fever, and sweats recur; evidently drainage has become insufficient and pus accumulates. Again, a large amount of pus may be discharged, and again the expectoration may cease; such variation in the phenomena (alternate emptying and refilling) may recur for some time until recovery eventually ensues or the patient dies. A second unruptured abscess should be suspected in the event of persistence of the septic phenomena, despite evident free drainage.

Rupture into the stomach or the duodenum is usually followed by epigastric distress, nausea, vomiting of considerable pus, diminution in the size of the liver, and perhaps relief of the local symptoms referable to the liver. Rupture into the intestine is followed by diarrhœa and pus in the stools; the pus frequently is overlooked, especially when the rupture occurs into the small intestine. Perforation into the peritoneum may occur into preformed adhesions, whence a localized extrahepatic abscess may ensue, or into the general peritoneal cavity, in which event a generalized peritonitis may be set up; but sometimes, in view of the

<sup>1</sup> *Traité pratique des maladies du foie*, 1887.

<sup>2</sup> *Cyclopædia of the Practice of Medicine*, v. Ziemssen, 1880, ix, 138.



fact that the abscess may be sterile, peritonitis may not immediately ensue and the patient, if operated upon, may recover.

**Diagnosis.**—This is often attended with considerable difficulty. The most suggestive signs are the etiological factors, which vary with the source of infection, but which should be carefully studied; pain in the region of the liver, perhaps referred to the right shoulder; progressive enlargement and tenderness of the liver; slight jaundice, and chills, fever, sweats, and leukocytosis. These symptoms, however, are not always outspoken; the leukocytosis, for instance, may be slight, and the so-called tropical abscess may be latent for a long time, and when somewhat active may give rise to quite indefinite symptoms.

Manson<sup>1</sup> states: "Golden rules in tropical practice are to think of hepatic abscess in all cases of progressive deterioration of health; and to suspect liver abscess in all obscure abdominal cases associated with evening rise of temperature, and this particularly if there be enlargement of or pain in the liver, leukocytosis, and a history of dysentery—not necessarily recent dysentery. If doubt exists, there should be no hesitation in having early recourse to the aspirator to clear up the diagnosis." "The most common mistakes in diagnosis are: (1) Failure to recognize the presence of disease of any description, even when an enormous abscess may occupy the liver. (2) Misinterpretation of the significance and nature of a basic pneumonia—a condition so often accompanying suppurative hepatitis. (3) Attributing the fever symptomatic of liver abscess to malaria. (4) Mistaking other diseases for abscess of the liver, and *vice versa*—for example, hepatitis of a non-suppurative nature; suppurative hepatitis before the formation of abscesses; syphilitic disease of the liver—softening gummata which are often attended with fever of hectic type; pyelephlebitis; suppurating hydatid; gall-stone and inflammation of the gall-bladder, subphrenic abscess; abscess of the abdominal or thoracic wall; pleurisy; encysted empyema; pyelitis of the right kidney; pernicious anemia; leukemia; scurvy and similar blood diseases associated with enlargement of the liver; ulcerative endocarditis; kala-azar; Malta fever; trypanosomiasis. Any of these may be attended with fever of hectic type, increased area of hepatic percussion dulness, and pain in and about the liver."

Malaria may be excluded by an evening rise in temperature (that of malaria being more common during the day); disproportionate enlargement of the liver as compared with the spleen (the reverse being the case in malaria); absence of malarial parasites in the blood; polynuclear leukocytosis; and the non-response to quinine. Cholelithiasis and Charcot's biliary intermittent fever may be excluded by the absence of a history of cholecystitis, cholelithiasis, and biliary infection; the absence of attacks of fever, etc., separated by longer or shorter periods of apyrexia; non-occurrence of increase in the jaundice after each attack; and the absence of serious impairment of the general health.

**Prognosis.**—The small multiple abscesses of the liver, whatever their etiology, are almost invariably fatal, death usually resulting within one

<sup>1</sup> *Tropical Diseases*, 1907, 4th edit., 510.

to three weeks. Many of the large single so-called tropical abscesses eventuate in recovery; their duration, however, is uncertain, since it is not possible always to say when they began; they are often latent for a long time. The mortality in unoperated cases has varied up to 80 per cent., but Cantlie states that now the figures "have fallen to between 20 and 30 per cent., and there is no doubt that with earlier operations the mortality will be still further reduced." The outlook after rupture into the lung and evacuation through a bronchus (hepatopulmonary abscess) is rather favorable (75 per cent. of recoveries, De Castro), although the condition may last for months; rupture into the hollow abdominal viscera or externally may also be followed by recovery; but rupture into the peritoneum, the pericardium, etc., is usually fatal. Recurrence of the abscess may follow apparent recovery.

**Treatment.**—This is essentially surgical in such forms as are amenable to treatment. The treatment of the multiple septicopyemic abscesses is that of septicopyemia in general; the liver condition neither modifies nor influences appreciably the treatment, which should be stimulating and supporting, with such drainage or other surgical treatment of the original focus of disease as may be possible. Rogers<sup>1</sup> has claimed remarkable results in amoebic abscess by the use of emetin hydrochloride or hydrobromide in  $\frac{1}{2}$  to  $\frac{1}{3}$  of a grain doses injected subcutaneously. He also believes emetin to be of distinct diagnostic value on account of the rapid improvement seen after its use in amoebic cases.

The diagnosis of the large single abscess furnishes the indication for its evacuation; and even when the diagnosis of a single abscess cannot be made positively, although hepatic suppuration is obviously present, resort should be had to operation. Manson, Cantlie, and others of much experience advocate evacuating the abscess by means of a trocar and cannula.<sup>2</sup> In the event of perforation of the abscess, immediate operation is indicated; operation is indicated also in the event of perforation into the lung, hollow abdominal viscera, etc., but it need not be undertaken immediately, since in many of these cases spontaneous recovery ensues; signs warranting delay consist of good general condition of the patient, minor septic or toxic phenomena, free discharge of pus, by the bowel or by expectoration, improvement in the local conditions, etc.

### CHRONIC INTERSTITIAL HEPATITIS: THE CIRRHOSES OF THE LIVER

Chronic interstitial hepatitis, comprising the so-called cirrheses of the liver, has been much and variously classified—etiologically, anatomically, and clinically.<sup>3</sup> The disorder was first described by Vesalius, but the term cirrhosis was first employed by Laennec to describe the yellowish "hobnails," which he regarded as new growth.

<sup>1</sup> *Brit. Med. Jour.*, 1912, ii, 405.

<sup>2</sup> The details of the procedure may be found in Manson, *loc. cit.*, and Cantlie, *Internat. Clin.*, Phila., 1904, 14th series, ii, 93.

<sup>3</sup> Consult Edwards, *Internat. Clin.*, Phila., 1902, 12th series, ii, 92.

Eliminating from consideration cases of: (1) So-called capsular cirrhosis (more properly called perihepatitis or hepatic capsulitis), in which the liver tissue may be not at all affected, except perhaps secondarily in consequence of compression or by slight ingrowth of new connective tissue from the capsule; (2) so-called cardiac cirrhosis or cardiac liver, which develops in consequence of long-standing passive congestion; (3) syphilis of the liver, in which the lesions are specific and peculiar to that infection; and (4) circumscribed or focal fibroses which follow limited inflammatory and degenerative processes, focal necroses, chronic obstruction of the biliary ducts (pericholangitis), etc., there are two types of chronic diffuse disorder of the liver, attended by fibrosis, to which the term cirrhosis may be limited. One of these disorders is very common; it is usually due to the misuse of alcohol; it is characterized by moderate enlargement of the liver (which in advanced stages may become reduced in size), by phenomena of portal obstruction (notably hematemesis and ascites), and by the absence or unimportance of jaundice; and after the development of symptoms it usually runs a comparatively short course (Laennec's portal, alcoholic, atrophic, or multilobular cirrhosis). The second of these disorders is rare; it is of unknown etiology; it is characterized by marked and persistent enlargement of the liver and spleen, by chronic jaundice, by periodic attacks of abdominal pain and fever, and by the absence of manifestations of portal obstruction (notably ascites); and it runs a comparatively long course (Hanot's, biliary, hypertrophic, or monolobular cirrhosis).

There can be no serious objection to the use of the terms Laennec's and Hanot's cirrhosis, aside from that inherent in eponymic terms. Alcoholic cirrhosis accurately describes most, but not all, cases of Laennec's cirrhosis; but alcohol perhaps sometimes gives rise also to Hanot's cirrhosis, although this is a disputed point, and the study of the etiological factors is important from many points of view, particularly the therapeutic. The terms atrophic and hypertrophic, to designate, respectively, a small and a large liver, are most ill-advised and have led to confusion and misapprehension. There has been much discussion as to whether or not there is a so-called hypertrophic stage of atrophic or Laennec's cirrhosis, and this so-called hypertrophic stage has been confounded with what is spoken of as hypertrophic or Hanot's cirrhosis. Aside from notable variations in size that may occur within a comparatively short time in a liver the seat of Laennec's cirrhosis, a small or so-called atrophic liver is often hyperplastic to a considerable degree, and a large or so-called hypertrophic liver always exhibits considerable atrophy of the hepatic parenchyma; and many cases of Laennec's cirrhosis result fatally while the liver is still larger than normally; that is, in many cases the so-called atrophic liver does not become atrophic (smaller than normally), but remains to the end, as it were, hypertrophic. The terms assuredly are inadequate to describe the conditions, and should be discontinued.

The preferable terms for the two main types of cirrhosis, of which there are subtypes, are portal and biliary; portal, because the etiological factor is perhaps always transmitted by the portal circulation, the new-



formed connective tissue is specially conspicuous in and about the portal spaces in the liver, and the obtrusive symptoms are those of portal obstruction; biliary cirrhosis, because the essential lesion is a radicular cholangitis and the conspicuous clinical feature is jaundice, due to obstruction to the free flow of bile.

Two subtypes of biliary cirrhosis are sometimes differentiated: (1) The hypertrophic biliary cirrhosis of Hanot; and (2) an obstructive biliary cirrhosis—by which is meant a condition of pericholangitic fibrosis spreading to the adjacent liver lobules in obstruction of the extrahepatic biliary ducts. The disorder was first described by Wickham Legg, and later by Charcot and Gombault, Gilbert and Sourmont, Chauffard, Ford,<sup>1</sup> Weber,<sup>2</sup> etc. There is no doubt that fibrosis does occur in the liver in some cases of chronic obstruction of the extrahepatic biliary ducts; but the fibrosis is usually minor in grade, develops about the intrahepatic biliary ducts (pericholangitis), seldom implicates the liver lobules to a noteworthy degree, and of itself does not give rise to noteworthy symptoms; the symptoms remain those of the obstruction (especially chronic jaundice and acholic stools), to which subsequently may be added, as in any disorder of the liver, phenomena attributable to disorganization of the hepatic parenchyma. Compression of the common bile duct, with complete interruption to the flow of bile, as occurs in carcinoma of the head of the pancreas, is often attended by serious consequences, such as dilatation of the intrahepatic ducts with rupture of the biliary capillaries leading to degeneration and necrosis in the centre of the lobule,<sup>3</sup> or to compression atrophy, degeneration, and pigmentation of the liver cells; in some cases also some replacement fibrosis occurs, but in degree it is by no means comparable to that of cirrhosis in the ordinary sense. The inference is that in most cases of considerable fibrosis of the liver in chronic obstruction of the biliary ducts, factors other than the obstruction are the real cause of the fibrosis. In some cases this is doubtless infection of the biliary tract, with connective cholangitis and pericholangitis, as occurs in some cases of cholelithiasis, with more or less incomplete obstruction; in other cases, the common causes of portal cirrhosis, such as alcoholism, disorders of the intestine (due in part perhaps to absence of bile), etc. The proper interpretation of the phenomena is of more importance and interest than attaches to academic discussions; those that interpret localized fibrosis as cirrhosis will continue to speak of the condition as obstructive biliary cirrhosis; but it is not beyond the facts to assert that biliary obstruction of itself does not give rise to cirrhosis in an acceptable sense, that the fibrosis that does occur is not of constant type, is almost negligible anatomically, and is assuredly negligible clinically, and that when a noteworthy cirrhosis occurs in association with obstruction to the biliary ducts it is probably due to the ordinary causes of cirrhosis rather than to the obstruction.

<sup>1</sup> *Amer. Jour. Med. Sc.*, 1901, cxxi, 60.

<sup>2</sup> *Trans. Path. Soc.*, Lond., 1903, liv, 103.

<sup>3</sup> Consult Ogata, *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1913, lv, 236.

**Portal Cirrhosis.**—Portal cirrhosis is a chronic degenerative and inflammatory disease of the liver characterized by recurring degeneration and regeneration of the hepatic parenchyma and by concomitant and consecutive fibrosis in and about the interlobular or portal spaces, all of which leads ultimately to obstruction of the portal circulation.

**Etiology.**—Portal cirrhosis is peculiarly a disease of adult life; it is most common during the fifth decade, the majority of the subjects succumbing before the fiftieth year, forty-eight and seven-tenths years being the average age of 121 males, and forty-seven years of 44 females, (Rolleston). It is, however, by no means rare at the extremes of life. A notable number of cases occur in young children, in whom it is often fatal before the sixth year. It is a little more than twice as common in men as in women; and it is also more commonly latent in men. Occupation is of significance only as it concerns other factors, notably alcoholism.

Portal cirrhosis is undoubtedly the expression of the activity of some poison or poisons; these are various in nature, and may reach the liver by way of the portal vein, the hepatic artery, or both. In the great majority of cases the portal vein is unquestionably the pathway. From time immemorial major importance has been attributed to alcohol, and assuredly with reason; but during recent years attempts have been made to minimize its influence, and its action is probably indirect rather than direct. Alcohol is especially active when taken in the form of distilled liquors, but cirrhosis occurs also in those addicted to the use of wine, beer, ale, porter, etc., and it is more common among those who drink constantly a small amount than among those who occasionally drink a considerable amount. The stronger liquors are the more active probably because they are often taken on an empty stomach and consequently reach the liver in concentrated form. How the alcohol acts is not definitely known, but it is likely that it acts: (1) As a direct irritant or poison to the liver cells (of which there is sufficient experimental proof), causing parenchymatous and fatty degeneration, even necrosis, or disturbing the functions of the liver cells and rendering them unduly susceptible to the influence of other causative factors (autogenic poisons, bacterial toxins, etc.), as well as irritating the connective tissue of the organ; and (2) by causing gastro-intestinal catarrh and thus favoring the formation of divers autotoxins inseparable from that condition which, transported by the portal vein, may be the active factor in provoking cirrhosis in a liver otherwise rendered vulnerable. It has been suggested that ethyl alcohol is not the active factor in setting up the cirrhosis, but rather adulterants, such as amyl alcohol, the aldehydes, aromatic substances, etc.; but as yet this is pure hypothesis. Certainly, however, cirrhosis occurs in the absence of alcoholism, and not all alcoholics become cirrhotic. In cases in which alcohol seems to be, or is, the only obviously active factor, it is not unlikely that there is also a concealed hereditary or a postnatal acquired lowered vitality on the part of the liver that renders it especially susceptible; and this is doubtless

true also in respect to other etiological factors.<sup>1</sup> That hereditary influence is sometimes operative is suggested by the occasional occurrence of several cases of cirrhosis in the one family; but in these cases one cannot overlook the likelihood of familial addiction to alcoholism, as well as hereditary syphilis.

There is reason to believe that poisons, particularly the fatty acids (lactic, butyric, acetic, valerianic, etc.) and other ill-understood enterogenic toxins associated with different forms of indigestion may be causative factors, especially in non-alcoholic subjects who give a history of long-continued indigestion, following or associated with overindulgence in highly seasoned foods, spices, etc. (dyspeptic cirrhosis, Budd's non-alcoholic cirrhosis). The fatty acids and other toxins rarely may be ingested preformed with the food; but they are much more likely to be manufactured in the intestinal tract in cases of gastro-intestinal catarrh (fermentative dyspepsia); experimentally lesions resembling those of cirrhosis have been produced by injecting fatty acids into lower animals. To the influence of enterogenic toxins, spices, etc., may also be attributed the cirrhosis occurring among the Hindus, Egyptians, etc., who, avoiding alcohol, nevertheless often eat food that is not above reproach and are quite partial to condiments and spices, such as ginger, pepper, etc., often in decoctions. It is also likely that a poison elaborated in the spleen may cause cirrhosis (Banti's disease).

Infections of various kinds may be followed by cirrhosis, but the relationship of the one to the other has not yet been definitely determined. In most of these cases the infection is carried to the liver by the general as well as by the portal circulation. Many acute infections are known to cause pathological changes in the liver (degeneration, focal necroses, inflammation, etc.), and some of these are followed by fibrosis—usually localized and minor or moderate in grade; but this scarcely constitutes cirrhosis in an acceptable sense. McCrae and Klotz<sup>2</sup> believe that the focal necroses occurring at times in typhoid fever are caused by toxins and that they do not contain bacteria. These changes may perhaps lead later to cirrhosis. A malarial cirrhosis has been widely commented upon, but it is probably not as common as many observers believe: both diseases may occur concurrently. Tuberculosis is sometimes associated with cirrhosis, especially fatty cirrhosis, and some observers believe that the tubercle bacillus or the tubercle toxin absorbed from the intestinal tract or the peritoneum may set up the lesions of cirrhosis.<sup>3</sup> The lesions in the liver caused by syphilis are not those of cirrhosis (in a restricted sense), but antecedent syphilis may render a liver unusually susceptible to the ordinary causes of cirrhosis. A form of cirrhosis occurring in Egypt and elsewhere has been attributed to a toxin

<sup>1</sup> Consult Kern's article on changes in the liver in chronic alcoholism (*Zeitschr. f. Hyg. u. Infektionskrankh.*, Leipz., 1912, lxxiii, 143) and Mathias Thiesen on Atrophic (Laennec's) Cirrhosis of the Liver (*Dissert.*, Strassburg, 1912). Both these articles contain interesting statistics gathered from a wealth of autopsy material upon the subject of the influence of alcohol on the liver.

<sup>2</sup> *Jour. Path. and Bacteriol.*, Cambridge, 1908, xii, 279.

<sup>3</sup> Consult Jagie, *Wien. klin. Wchnschr.*, 1907, xx, 849; Stoerk, *ibid.*, 1907, xx, 1011, 1048; and Isaac, *Frankf. Zeitschr. f. Path.*, Wiesbaden, 1908, ii, 125.



elaborated by *Uncinaria duodenalis* and *Bilharzia hæmatobia*, with which these subjects are infected. Rogers<sup>1</sup> has described a peculiar form of intralobular cirrhosis produced by the protozoal parasite of kala-azar. Adami's observations relating to a so-called diplococcic form of the colon bacillus in cirrhosis in man and in infective cirrhosis in cattle is of interest, not so much as suggesting an etiological relationship of the bacterium to cirrhosis, but as illustrating the bactericidal properties of the liver cells. It is not improbable that bacteria may be indirectly the cause of cirrhosis in setting up catarrhal and fermentative processes in the intestine, the toxic concomitants of which, being transported to the liver, may act as the direct irritant factor.

Other sorts of irritants sometimes appear to give rise to cirrhosis. Thus in hemochromatosis, in consequence of hemolysis, blood pigment is set free and infiltrates the tissues, and the liver and the pancreas become fibrotic. Cirrhosis of the liver has been found in association with pneumokoniosis, and with poisoning with lead, silver, arsenic, etc.

Experimentally,<sup>2</sup> so-called cirrhosis, but usually minor and circumscribed fibrosis, has been produced by injecting certain bacteria, alcohol, and other irritants, such as chemicals, vegetable alkaloids, etc., into the portal circulation, the general circulation, and the intestine. Much more significant and of more importance are Pearce's<sup>3</sup> studies regarding the effects of hemolytic and hemagglutinative sera: the early necrotic lesions in the liver are followed by reparative processes that constitute a chronic interstitial hepatitis; these are of special interest, since they demonstrate that cirrhosis may follow widespread destruction of necrotic lesions in the liver, and explain the histogenesis of cirrhosis and other reparative processes in the liver. Opie<sup>4</sup> has demonstrated that cirrhosis of the liver can be experimentally produced by administering chloroform by mouth and injecting bacteria into the blood.

**Pathology.**—The liver varies much in size in different cases, and in the same case at different times. At the necropsy it may be very small, weighing only 970 grams or less; or it may be very large, weighing as much as 4000 grams or more; but in the majority of cases at autopsy it weighs more than normally. Rolleston states that the average weight of the liver in 155 consecutive necropsies on cirrhotic subjects at St. George's Hospital was 63.6 ounces (1778 grams); the average weight of the liver in 100 cases collected by Hawkins was 52 ounces (1617 grams), the minimum being 32 ounces (995 grams), and the maximum 74 ounces (2300 grams); the average weight in 93 cases collected by Kelynack was 53 ounces (1648 grams); and the average weight in 34 cases at the German Hospital, Philadelphia, was 1875 grams, the minimum being 980 grams and the maximum 2760 grams. In fatal cases in young subjects the liver is relatively and often absolutely larger than in older subjects.

Variations in the size may be due to different factors. It is essential to bear in mind that in the usual course of events the liver may be

<sup>1</sup> *Ann. Trop. Med. and Parasitol.*, Liverpool, July, 1908.

<sup>2</sup> Consult Fischler, *Deutsch. Arch. f. klin. Med.*, Leipz., 1908, xciii, 427.

<sup>3</sup> *Jour. Exper. Med.*, 1906, viii, 64; *Jour. Med. Research*, 1906, xv, 99 (literature).

<sup>4</sup> *Jour. Exper. Med.*, 1910, xii, 367.

enlarged from the beginning to the end of the disease. It is often said that the liver is enlarged in the early stages and small in the later stages—in consequence of contraction of the newly formed fibrous tissue. This change in size is sometimes observed, but it is incorrect to assume that the decrease in size is due always or solely to contraction of the new fibrous tissue. Marked variations in size often occur rapidly, within several days or weeks, and are due solely to changes in the vascular supply. The writer saw a liver a handbreadth below the costal margin in the nipple line lessen so rapidly in size that at operation, two weeks later, it had receded well above the costal margin and presented the typical appearances of portal cirrhosis. A liver small at one clinical examination may be much enlarged subsequently. The large liver may be due to vascular engorgement, hyperplasia of the liver cells, disproportionate fibrosis that is likely to be diffuse, as in the so-called monolobular type, and fatty infiltration and degeneration of the liver cells (fatty cirrhosis).

As a rule, the liver is of increased density (increased specific gravity), so that a small liver may weigh more than a liver of normal size; it is of increased consistency and lessened elasticity. The capsule is often opaque, sometimes considerably thickened, and not infrequently adherent to the under surface of the diaphragm. Adhesions, when present, are usually old, fibrous, and circumscribed rather than widespread; occasionally, however, they are almost if not quite universal and may extend to adjacent organs—the gall-bladder, stomach, intestine, omentum, through the diaphragm to the pleura, lung, etc. In other cases more or less recent, acute, fibrinous adhesions are encountered.

The *surface* of the liver is distinctly granular, the small livers more so than the larger ones: grayish-white opaque depressions alternate with pale, yellowish-brown, sometimes reddish-brown, roundish or ovoid elevations—the so-called granular or “hobnail” liver. The hobnails vary considerably in size, from those scarcely larger than a pinhead (under which circumstances the surface of the liver is comparatively smooth) to others 1 to 2 cm. in diameter; usually they average from 2 to 4 mm. in diameter. Sometimes many—ten or more—hobnails appear specially surrounded by an unusually wide band of connective tissue that isolates them from adjacent tissue and causes a more marked projection from the general surface of the organ. These lesions usually are distributed uniformly throughout, but occasionally one lobe is more involved than the others; the left lobe especially may be very small (lessened resistance?); rarely the caudate, quadrate, or Spigelian lobe may be disproportionately affected.

On section the liver cuts with increased resistance, being much denser, firmer, and tougher than normally. The cut surface reveals interlacing bands of whitish or grayish-white fibrous connective tissue that vary somewhat in thickness, pervade the entire organ, and are continuous with the grayish opaque depressions on the surface. These bands, which obviously take their origin in the periportal spaces, form a network that encloses or surrounds islets of liver tissue that vary in size from that of a pin-point to others 1 cm. or more in diameter; the larger islets

are made up of several, often eight, ten, or more, liver lobules (or remains of liver lobules), and are pervaded by more delicate bands of connective tissue (so-called multilobular cirrhosis). In many, but not all, cases the islets of liver cells appear to be under some tension, since on section they project somewhat; it is not improbable that this is due to the elastic tissue of which in part the newly formed connective tissue consists. The liver tissue is usually pale yellowish in color or yellowish brown; occasionally it is greenish (from staining with bile), or reddish or brownish, especially in the centres of the lobules (from staining with blood or blood pigment). The islets of liver tissue are sometimes very large, hyperplastic, evidently the result of active proliferation, a condition sometimes spoken of as nodular cirrhosis, or cirrhosis with multiple adenoma. This process, doubtless at first compensatory, sometimes becomes unrestrained and results in the production of carcinoma (cirrhosis with carcinoma). Occasionally the islets of liver tissue are very pale (fatty degeneration) and at first sight resemble new-growth; in some cases the centres of some of the nodules are quite soft and necrotic.

The bloodvessels show more or less well-marked changes. The hepatic artery and its smaller branches are often distended—doubtless related to the necessity of supplying with blood the increased fibrous tissue; in some cases the vessels exhibit the ordinary lesions of endarteritis, especially in the cirrhosis of hemochromatosis and of syphilis. The hepatic veins may show the lesions of obliterating endophlebitis, as has been pointed out by Hess.<sup>1</sup> The smaller intrahepatic branches of the portal vein, especially those between the liver lobules, are often compressed and not infrequently thrombosed; the larger intrahepatic branches, the main trunk, and the gastro-intestinal branches that go to form the main trunk are usually dilated; the wall of the vein is often thickened—periphlebitis and endophlebitis; and thrombosis of the main trunk may occur (more common in cirrhosis than in any other condition).

Communications between the portal vein and the systemic circulation constitute a part of the cirrhotic process. For the most part these consist of dilatations of normally existing anastomoses. They subserve the useful purpose of diverting to the superior and the inferior venæ cavæ the venous blood in the portal tributaries flowing against the obstruction in the portal distribution in the liver, and thus they relieve the portal congestion. Although usually present, they are not always observed; they are sometimes absent in fatal cases of cirrhosis in which death has resulted from other causes.<sup>2</sup> Through increased pressure in the portal circulation various anastomoses become dilated, thus giving passage to the venous blood obstructed by the cirrhotic liver. Various compensatory anastomoses occur. Rolleston considers them under the heading of (1) general and (2) local.

1. *General communications* between the retroperitoneal veins opening into the lumbar and azygos veins, and the veins of the peritoneum and of the intestines. Also branches of the portal vein anastomosing with

<sup>1</sup> *Am. Jour. Med. Sc.*, 1905, cxxx, 986.

<sup>2</sup> For an excellent study with a review of the literature consult also Gilbert and Villaret, *Rev. de méd.*, Par., 1907, xxvii, 305.



the inferior vena cava, as described by Retzius, producing at times an intense injection of a large part of the parietal peritoneum. The Talma operation, frequently tried in cases of cirrhosis, attempts surgically to produce a similar collateral circulation.

2. *Local*.—Internal portocaval anastomoses developing in the lobules of the liver between branches of the portal vein and the intralobular vein. Communications may develop between the veins in the substance and capsule of the liver and the phrenic and intercostal veins, where the liver and diaphragm are uncovered by peritoneum. In addition a large vein running to the umbilicus in the falciform ligament may communicate with the veins of the abdominal wall, thus connecting the portal vein with the deep epigastric and external iliac veins, producing a "Caput Medusæ" most marked around the umbilicus. The veins of the œsophagus, which open into the azygos veins, communicate at the cardiac orifice with the gastric veins and so with the portal vein. In this way œsophageal varices are formed from which hemorrhages may occur. In cases of ascites with obstruction of the inferior vena cava a "Caput Medusæ" also occurs, due to enlargement of the veins of the skin connecting with the superior and inferior epigastric veins. Here the dilated veins run from the middle of the groins to the costal arches and avoid the umbilicus.

These anastomoses serve both a useful and an evil purpose. On the one hand, as long as the collateral circulation is efficient, obstructive symptoms are in abeyance and the liver is enabled better to perform its functions, perhaps enabled to regenerate, whence in some cases the disease remains or becomes latent, even apparently cured; on the other hand (*a*) the dilated veins are likely to rupture, either spontaneously or in consequence of trauma, and lead to more or less severe hemorrhage (hematemesis, hematoma of the abdominal wall about the round ligament); and (*b*) much of the blood from the gastro-intestinal tract being thus diverted from the liver to the general circulation, conditions somewhat analogous to those induced by the establishment of an Eck fistula supervene, much of the product of digestion is not brought under the influence of the liver, is not detoxified, and toxemia ensues.

The gall-bladder and the biliary ducts are usually normal; occasionally there is some thickening of the wall of the gall-bladder from chronic cholecystitis. Calculi are sometimes encountered in the gall-bladder or the ducts: in 21 (15.4 per cent.) of 136 fatal cases (Rolleston); in 18 (8.6 per cent.) of 209 men, and in 7 (17 per cent.) of 41 women (Klopstock); in 8 (22.2 per cent.) of 36 cases at the German Hospital, Philadelphia.

**Histology.**<sup>1</sup>—A clear conception of the cirrhotic process is best attained by bearing in mind that, as emphasized by Kretz,<sup>2</sup> the liver is not made up of acini in an acceptable sense. While the physiological unit is that

<sup>1</sup> This is largely an abstract of an article by A. O. J. Kelly, entitled *The Nature and the Lesions of Cirrhosis of the Liver, with Special Reference to the Regeneration and Rearrangement of the Liver Parenchyma*, *Am. Jour. Med. Sc.*, 1905, cxxx, 951.

<sup>2</sup> *Ueber Lebercirrhose*, *Wien. klin. Wchnschr.*, 1900, xiii, 271; *Verhandl. d. deutsch. path. Gesellsch.*, Berl., 1904, viii, 54; *Internat. Clin.*, Phila., 1905, iii, 289.

collection of cells drained by a radicle of the bile duct, this unit is scarcely delimitable anatomically; nor are the so-called acini, or lobules, cross-sections of which, surrounded by connective tissues, form such a conspicuous feature of microscopic sections, of such simple structure as at first appears. Study of the liver in serial sections and its reconstruction show that the liver parenchyma does not form isolated acini, or lobules, everywhere surrounded by connective tissue, but that what appear to be acini are merely cross-sections of liver cells arranged as a mantle about the numerous dendritic ramifications of the hepatic vein, and that this mantle is nowhere discontinuous, forming, on the contrary, a continuous whole, everywhere connected, particularly at the points of junction of the sublobular, lobular, and lobar veins. The intimate relationship that the liver cells structurally bear to the hepatic vein is further shown by the radial disposition of the cells about the branches of this vein—the so-called central veins.

As distinguished from most other organs, the liver has two sources of blood-supply—the portal vein and the hepatic artery—which commingling form a plexiform capillary network, in the meshes of which the liver cells are arranged. Ultimately, the capillaries unite again to form the radicles of the hepatic vein—the rectilinear veins of Sabourin which empty into the so-called central veins. The circulation within the liver, which is of much importance in connection with certain features of cirrhosis, has been studied attentively by Opie.<sup>1</sup> It has long been known, and Opie especially has directed attention to the fact that one of the important characteristics of the liver is its susceptibility to variations in blood-pressure, saying: "The portal vein, hepatic artery, and hepatic vein are in such free communication that the entire lobule can be injected from any one of these vessels. Hence artificial injections do not define the intralobular distribution of the portal and arterial blood, for doubtless differences of venous and arterial pressure have a part in determining peculiarities of the circulation within the lobule." Opie's experimental studies led him to the conclusion "that both the hepatic artery and portal vein pour their blood into the periphery of the lobule, and here the influence of the arterial blood-pressure is most strongly felt. When foreign material reaches the liver by the portal vein it is washed from the peripheral zone by the arterial blood, and tends to be deposited in a middle zone, where the influence of the opposing circulation is less strongly felt. Hence it is not improbable that toxic substances capable of causing necrosis of the hepatic cells, brought to the liver by the portal vein, might first exert their effect upon cells within a midlobular zone. The periphery of the lobule, moreover, is supplied with arterial blood, and is perhaps for this reason less susceptible to injurious agencies."

If the parenchyma of the liver in a moderately advanced or well-advanced case of cirrhosis is studied attentively, certain noteworthy deviations from the normal become apparent—changes in the size, shape, and configuration of the lobules, and in the arrangement of the liver

<sup>1</sup> *Jour. Med. Research.*, 1904, xii, 147.

cells; degenerative, atrophic, and hyperplastic changes in the liver cells; changes in the vascular arrangement and supply.

The size of the lobules or "hobnails" in cirrhosis has been studied by Kretz,<sup>1</sup> MacCallum,<sup>2</sup> etc. Kretz has shown that the normal lobules are roundish polygonal in shape, with their long axes in the direction of the central vein, and (as is well known) that their greatest diameter is usually a little more than 1.5 mm., and may reach 2.5 mm., whereas the short diameter is about 1 mm., and that in cirrhosis these figures are surpassed, some lobules being much larger, and other collections of cells much smaller. MacCallum found that while the average radius of a lobule (that is, the thickness of the mantle of cells about the central vein) in a number of normal livers is about 0.66 mm., in advanced cirrhosis lobules are encountered that measure, from central vein to periphery, 1 mm. or more, the small diameter, therefore, being more than 2 mm.

There is a notable departure from the normal shape and configuration of the lobules; many of them are no longer rounded, but quite irregular in transverse section; many of the cell mantles no longer surround the central veins equally on all sides, but very unequally, so that many central veins are situated eccentrically in a more or less misshapen lobule; many so-called lobules have no central vein at all (and are not tangential sections of otherwise normally arranged lobules); certain lobules (or so-called lobules, usually remains of several) have two, three, four, or more central veins; and often the central vein may be seen in the adjacent interlobular connective tissue. Thus the mantle of cells covering a central vein varies much in thickness in different regions (transverse planes), sometimes exposing, sometimes covering, the vein to a greater or less extent; and although isolated collections of liver cells (that is, collections devoid of central veins) do occur, some supposedly isolated collections are merely sections of more or less irregularly proliferating dendritic branches of what may be called the parent stem, or mantle covering a single central vein.

Furthermore, although the normal radial arrangement of the liver cells about the central vein is preserved to some extent, in many places it is totally wanting; the architecture of the lobule has become altered so that the cells are arranged irregularly in parallel rows, etc. This is quite as well-marked in many of the lobules that have a central vein as in those collections of cells entirely devoid of central veins.

The parenchymatous cells show various degenerative changes. In the early stages many cells become degenerated, necrotic, and are removed, but from the nature and the stage of the process at which this occurs, it is rarely observed, except in cases that run a rapid course and in certain cases of pigmented cirrhosis. In some cases there is considerable or widespread fatty infiltration (so-called fatty cirrhosis). In advanced cases considerable atrophy of the liver cells may be observed.

Evidences of *hyperplasia* of the liver cells are readily found in almost every cirrhotic liver, even in far-advanced cases. Mitoses are rarely encountered in advanced cases—largely in consequence of the nature

<sup>1</sup> Loc. cit.

<sup>2</sup> *Jour. Am. Med. Assn.*, 1904, xliii, 649.



of the process, the advanced stage at which the examination is generally undertaken, and the length of time after death that the liver is obtained, time sufficient for the completion of any mitoses present at death. That many of the liver cells are newly formed is quite apparent from their large, clear, and plump appearance, their rounded (rather than polygonal) outline, the presence of two or more nuclei, and the absence of fat and of pigment from their protoplasm. These cells, sometimes small collections of them, are situated amidst other liver cells normal in size and outline, provided with only a single nucleus each (though sometimes with two nuclei, which is quite normal), and the protoplasm of which is normally pigmented and contains fat. These newly formed cells are usually found at the periphery of a lobule; sometimes they make up a larger or smaller sector of a lobule; sometimes they seem to have compressed the older cells in their immediate vicinity; and sometimes small collections of them are found completely surrounded by wide bands of connective tissue. It is, however, probable that liver cells always regenerate from preëxisting liver cells. Necrotic and hyperplastic changes may be found in the one lobule.

A characteristic feature of almost all cases, more conspicuous in some cases than in others, is the bile-ducts or so-called pseudobiliary canaliculi, the nature and origin of which has occasioned much discussion. Doubtless the great increase of these structures in cirrhosis, as contrasted with the normal liver, is relative only, and due in part, but only in small part, to mutual approximation of already existing bile ducts occurring in consequence of loss of the liver tissue; but that most of them are newly formed is generally conceded, and is quite apparent from their excessive number and the evidences of active proliferation (mitosis) that they commonly exhibit. Their origin has not been determined definitely for all cases. It seems quite certain that some of them, at least, result from proliferation of previously existing bile ducts; on the other hand, since they are found in a wide variety of disorders, such as all forms of cirrhosis, acute yellow atrophy, in the neighborhood of hydatid cysts, tubercles, gummas, etc., in other words, in diseases alike only in that they destroy liver tissue; since they differ from normal bile ducts in the absence or relative paucity of encircling elastic tissue; since they have been found by Ackermann and others to be directly continuous with liver cells; and since in cases in which the liver cells have been much destroyed they are found in large numbers in what may be interpreted as the remains of the skeleton of the lobule, we are quite warranted in the opinion that they may result from proliferation of the liver cells themselves, constituting in this event a reversion to a less highly specialized type of structure. The important fact to point out is the histogenetic equivalence of the liver cells and the epithelium of the bile ducts, and the fact that proliferative changes of the liver parenchyma are a conspicuous feature of common cirrhosis.

The changes in the *connective tissue* vary with the stage and activity of the process. Early there is more or less round-cell infiltration in and about the portal spaces; later there is considerable increase in the amount of connective tissue—in part the result of organization of the

inflammatory exudate, in part a replacement fibrosis to fill up potential lacunæ left by destroyed liver parenchyma. This newly formed connective tissue commonly encloses rather than invades the liver lobules; sometimes only one lobule is enclosed in a wide band of connective tissue, sometimes many lobules—whence the designation *multilobular* cirrhosis.

A conspicuous change is the great increase in the elastic tissue—probably more or less intimately related to the great increase in the capillaries derived from arterioles; this elastic tissue not only makes up a large part of the fibrous bands between the lobules, but it is also found to some extent within the lobules, and occasionally a very small amount of it is found about or in the immediate neighborhood of the central veins.<sup>1</sup> A not inconsiderable part of the fibrosis is made up of reticulum—not only the reticulum normally between the lobules, but the intralobular reticulum—that remaining after the liver cells have degenerated and been removed.

*Lesions in other Organs.*—The *spleen* is enlarged in at least 80 per cent. of the cases (198 of 250 cases, Klopstock;<sup>2</sup>) it is probably enlarged some time during the course of all cases, but variations in size are due to different factors. There is no constant relationship between the size of the liver and of the spleen. At the necropsy the average weight of the spleen is about 400 grams; the average weight of 32 cases at the German Hospital, Philadelphia, was 400 grams, the minimum 110 grams, and the maximum 1320 grams. In the early stages, in consequence of increased vascularity, proliferation of the splenic pulp, and hyperplasia of the endothelial cells of the sinuses, the organ is about normal in consistency; later it becomes firmer and harder, in consequence of increase of the trabeculæ and consecutive atrophy of the lymphoid elements, particularly the Malpighian bodies. Considerable diminution in the size of the spleen may follow gastro-intestinal hemorrhage, severe diarrhœa, etc. Chronic perisplenitis occurs in about one-third of the cases; it may be localized or generalized.

The enlargement of the spleen is usually thought to be due to two factors: (1) Toxemia, bacterial or other toxins brought to the organ by the general circulation—which is especially operative during the early stages, since enlargement is not frequently observed early, before there is any evidence of portal obstruction; and (2) passive congestion—which is especially operative, although not the sole factor, in the later stages; undoubtedly it distends the blood spaces, and, obstructing the return circulation, it serves to retain irritating poisons in the organ. Hartwich<sup>3</sup> believes the hypertrophy to be compensatory.

The *gastro-intestinal tract* shows lesions due in part to the cause of the cirrhosis (alcoholism especially), in part to portal obstruction. The œsophagus shows general congestion, thickening of the mucosa, and in 80 per cent. of cases, dilated and tortuous veins, especially toward the lower end; these not infrequently rupture and cause severe and even

<sup>1</sup> Consult Milne, *Jour. Path. and Bacteriol.*, Cambridge, 1909, xiii, 362.

<sup>2</sup> *Arch. f. path. Anat.* (etc.), Berl., 1907, clxxxvii, 111.

<sup>3</sup> *Deutsch. med. Wchnschr.*, 1912, xxxviii, 1087.

fatal hemorrhage. The *stomach* is the seat of chronic gastritis, often associated with small superficial ulcers or abrasions; pigmentary infiltration, especially toward the pylorus; and dilated veins, especially toward the cardia; these also frequently rupture. The intestines reveal the ordinary lesions of chronic passive congestion and chronic enteritis with pigmentation. The rectum is often congested and the seat of small superficial ulcers and of dilated veins (hemorrhoids), both of which may lead to more or less severe hemorrhage. The *peritoneum* usually shows dilatation of the bloodvessels; often it is inflamed and chronically thickened, participating, on the one hand, in causing the ascites, and on the other hand, leading to thickening and distortion of the omentum and the mesentery with consecutive thickening and shortening of the small intestine (a reduction of eight to ten feet in length may occur). *Tuberculous* infection of the peritoneum is common, occurring in 9 per cent. of the fatal cases (Rolleston), and being more common in cirrhotic males than in other male subjects. It is often responsible for the fatal issue. It is sometimes latent and found only at the necropsy; in other cases it dominates the clinical picture. Roque and Cordier<sup>1</sup> maintain that every case of ascites occurring in portal cirrhosis is of tuberculous nature. The *pancreas*<sup>2</sup> is enlarged, swollen, and fibrotic, but there is no constant relationship between the size and the degree of fibrosis of the pancreas and of the liver; the parenchymatous cells show fatty degeneration and pigmentation; the islands of Langerhans are intact, except in the cirrhosis of hemochromatosis, in which they become destroyed.

The *kidneys* show deviations from the normal in about half of the cases. In most of these cases they are simply enlarged—doubtless the result of overwork (excessive drinking on the part of the patient, and efforts to remove toxic substances circulating in the blood); or they exhibit the lesions of chronic passive congestion (failure of the heart). In some cases, and usually early, albuminuria is encountered; later, distinct fibrosis occurs in 25 per cent. of the cases (110 of 440 cases collected by Rolleston). Few of these cases are due to the cirrhosis *per se*; both are usually due to a common cause (alcoholism), and both, as well as arteriosclerosis, occur at the same period of life and predominantly in the male sex. There is no constant relationship between the degree of fibrosis and the size of the kidneys and the liver.

The *heart* is often fibroid and fatty (alcoholism, arteriosclerosis), and consequently dilated. Endocarditis may occur as an accidental complication and the pericardium may contain a considerable excess of fluid (partly inflammatory, partly transudation). Arteriosclerosis is common, occurring in more than 60 per cent. of cirrhotic subjects; but it is not due to the cirrhosis (the blood-pressure is low in cirrhosis); both are more likely due to common causes—alcoholism, etc.

The *lungs* exhibit no characteristic lesions; but with the peritoneum they constitute the most frequent seat of tuberculosis in cirrhotic subjects. The tuberculosis may be acute or chronic, latent or obvious; and it leads directly to death in from 12 to 15 per cent. of the cases of cirrhosis

<sup>1</sup> *Rev. de méd., Par.*, 1912, xxxii, 761.

<sup>2</sup> Consult Lando, *Ztschr. f. Heilk.*, 1906, xxvii, 1.



(Rolleston). Right-sided pleuritis, due to transport of inflammation through the diaphragm from a perihepatitis, occurs in about 10 per cent.

**Pathogenesis.**—In portal cirrhosis, in consequence of the activity of some poison, larger or smaller areas of the liver tissue, that is, of the cell mantles about the central veins, become necrotic and are removed—whereby the central veins become more or less uncovered, thus on cross-section appearing eccentrically situated in more or less misshapen lobules; in some cases in which the destruction of liver cells has been through the entire radius of the cell mantle, the central vein may be entirely exposed and may even be found in the interlobular connective tissue, in which event it is very likely to be mistaken for a branch of the portal vein. The cells destroyed are those about the periphery of the lobules—in the area of portal distribution, conforming to the fact that the etiological factor is usually carried by the portal vein. Following the primary destruction of certain liver cells, the intact cells, exhibiting a remarkable regenerative capacity, attempt to replace the lost cells and sometimes succeed in restoring more or less completely the volume of the cell mantles. The cells that regenerate are those in the immediate vicinity of those that have become necrotic, that is, in the ordinary case in which the destruction is not widespread, cells toward or at the periphery of the lobule—which thus are not only most exposed to the deleterious influence of poisons carried by the circulation, but in consequence of being better supplied by arterial blood are also better adapted for repair. Kelly was inclined to believe, in view of Opie's researches, that the primary destructive action may be exerted, at least sometimes, in the so-called midlobular zone—at all events, not immediately at the periphery; that the peripheral cells, being better supplied with arterial blood, survive when others nearer the centre of the lobule succumb, and that these peripheral cells also serve as a focus of regeneration, although, of course, the cells nearer the centre of the lobule also regenerate.

The continuing activity of the etiological factor leads to a continuous or recrudescing death of certain old as well as newly formed liver cells, which in turn is followed by renewed regeneration. This continuous degeneration and regeneration ultimately lead to complete transformation of the architecture of the liver; certain lobules are entirely destroyed, others are partly or completely rearranged, some are markedly hyperplastic although tolerably well arranged, some show dendritic and other irregular proliferation, new islets of liver tissue entirely devoid of central veins appear, and, what is especially important, new circulatory conditions—capillary and venous—arise.

Concurrent with the degeneration of the liver cells, the framework of the lobules collapses and participates in the formation of the fibrosis. This ultimately contracts, and on the one hand causes atrophic changes in the liver cells, and on the other obstruction and obliteration of some of the interlobular and intralobular branches of the portal vein; this latter, although it contributes to, is not the sole cause of, the ascites—other important factors being the new circulatory conditions, especially certain changes in the hepatic arterial supply. Ultimately the potentiality for regeneration possessed by the liver cells lessens, and is finally

lost, the general functional capacity of the cells being meanwhile compromised by the contracting connective tissue; the degenerative changes predominate over the regenerative, and the patient dies, if he has not succumbed earlier to an accidental infection.

**Symptoms.**—Cirrhosis of the liver may remain for many years entirely latent; indeed, in most cases the lesions in the liver are well advanced before the onset of noteworthy symptoms, and the disease not infrequently constitutes an unexpected finding at the necropsy table. Symptomatically the disease has been divided into the pre-ascitic and the ascitic stage; and the symptoms are described as being (1) obstructive and (2) toxic. As long as the collateral circulation is efficient obstructive symptoms are in abeyance.

In a few cases, during the early stages, phenomena attributed to an ill-defined, so-called, active hyperemia of the liver are encountered; that is, the patient complains of ill-defined or vague gastric symptoms, a sense of weight in the right hypochondrium, perhaps short transitory attacks of slight fever, slight jaundice, and actual pain in the region of the liver, which on examination is found enlarged and tender. Such attacks may last several days, disappear, and recur at intervals.

In most cases the early symptoms are an expression of gastro-intestinal catarrh—due partly to portal congestion, and partly, in many cases at least, to chronic alcoholism with acute exacerbations. The patient complains of coated tongue, irregular appetite, flatulence, epigastric distress, especially after eating, sometimes of nausea and vomiting (often in the morning and usually referable to alcoholism), irregular action of the bowels (alternating attacks of diarrhoea and constipation), or habitual constipation, hemorrhoids, etc. The increasing portal obstruction leads to increasing congestion of the gastro-intestinal tract and the spleen, the congestion being doubtless favored by the absence of valves in the portal tributaries. This congestion reduces the functional capacity of the stomach and intestines, limiting the digestive juices and the intestinal secretions (although sometimes increasing the mucus), reducing the absorbing power of the intestines, and often inhibiting peristalsis. Constipation increases and tympanites not infrequently ensues, and both may become of high grade and distressing; occasional relief is sometimes afforded by attacks of diarrhoea which relieve the engorged vessels. These phenomena, while not diagnostic, are highly suggestive of the disease, especially with a history of alcoholism.

With the progress of the disease the foregoing evidences of derangement of the gastro-intestinal tract become more marked, and the general health becomes impaired; but the first obtrusive manifestation is not infrequently hematemesis or ascites.

*Hematemesis* is an initial symptom in some cases, and it is a common event some time in most cases. Usually it occurs early—while the liver is large; when not the initial symptom, it is often the first evidence of serious disease (33 per cent. of the cases); but it may occur late, that is, after the development of ascites and when the liver may have become small. The vomiting of blood may come on without warning, especially when the bleeding occurs from oesophageal varices and the blood does

not enter the stomach; in some cases it is preceded by distress or pain and faintness, particularly when it comes from the stomach; severe collapse is uncommon; an immediately fatal result is unusual, but it does occur: in one-third of 60 fatal cases collected by Preble<sup>1</sup> the first hemorrhage was fatal. The hemorrhage, as a rule, is large and consists usually of dark, partially clotted blood. A second or a third hemorrhage may occur at short intervals, and perhaps lead directly to death; or repeated hemorrhages may occur for years, eleven years being the maximum (Preble). The hemorrhage may be derived from: (1) Rupture of varicose veins in the œsophagus. These were present in 80 per cent. of the cases collected by Preble; in more than half of these the point of rupture was obvious to the naked eye, but in only 60 per cent. of the cases with œsophageal varices were there the typical signs and symptoms of cirrhosis. (2) Rupture of varicose veins of the stomach, which usually are situated near the cardiac end; the bleeding is sometimes profuse and may lead to a fatal termination. (3) Gastritis, in which event the hemorrhage is due to oozing from distended capillaries and venules. (4) Abrasion of the gastric mucosa, which may proceed to definite ulceration, and is often associated with gastritis. If the hemorrhage does not soon lead to death, it is an important factor in the development of anemia.

With the hematemesis there is usually blood in the stools; but blood may occur in the stools without the vomiting of blood, especially when the bleeding into the stomach is slow, and also when the source of the blood is the intestine, the rectum or hemorrhoids.

Hemorrhage from or into other parts of the body is very common. The tendency of cirrhotic subjects to bleed independently of stasis and the presence of jaundice is well known, and is justly attributed to toxemia with disturbed nutrition, the result of functional insufficiency of the liver. Whipple<sup>2</sup> has demonstrated that there is a low fibrinogen content of the blood. This is doubtless the underlying factor in some of the gastrointestinal hemorrhages and in much of the other hemorrhages. Epistaxis and bleeding from the gums are very common. Sometimes the amount of blood lost is large; it may occasion a well-marked anemia, and has proved fatal. Not infrequently the blood is carried to the fauces or pharynx, and, being then spat out, may simulate hemoptysis. The larynx occasionally exhibits varices (usually associated with œsophageal varices) which rupturing may lead to severe hemorrhage or a fatal issue. Bleeding from the lungs is not uncommon. Menorrhagia and metrorrhagia occur particularly in the early stages. Hemorrhages, usually petechial, into or beneath the skin, the mucous membranes and the serous membranes (pleura, pericardium, peritoneum) are not rare, although not so common as in biliary cirrhosis.

*Jaundice* is not a part of portal cirrhosis, but it occurs as a complication some time during the course of from 15 to 20 per cent. of the cases. A faint subicteric hue to the conjunctiva and the skin is not uncommon; it may come and go repeatedly, and last a longer or shorter time; it is usually due to a radicular cholangitis, and has been attentively studied

<sup>1</sup> *Am. Jour. Med. Sc.*, 1900, cxix, 263.

<sup>2</sup> *Arch. Int. Med.*, 1912, ix, 390.



by Naunyn.<sup>1</sup> More marked grades of jaundice attributable to catarrhal inflammation of the biliary ducts are occasionally observed. In the terminal stages more or less marked jaundice may result from associated catarrh of the biliary ducts, duodenal catarrh, compression or kinking of the ducts, or degenerative changes in the liver cells, and the changes of acute yellow atrophy.

Toxic symptoms may develop at any time during the course. They are much less common early than late, but are occasionally observed early in cases that for some time pursue a latent course. Minor symptoms consist of restlessness, weakness, headache, and itching; the itching may precede or be unassociated with jaundice. More severe toxic symptoms comprise: (1) Apathy, stupor, and coma; (2) an active noisy delirium; and (3) convulsions, paralyses, contractures, one of which may alternate with the others. These phenomena much resemble and are often mistaken for those due to uremia; in fact, they are not infrequently related to renal insufficiency.

Cirrhosis of the liver may be afebrile throughout its course; during the terminal stage the temperature may be subnormal; but attacks of fever ( $100^{\circ}$  to  $102.5^{\circ}$ ) are not uncommon. Sometimes these seem to be part of the disease, especially when it advances rapidly; sometimes they are due to attacks of perihepatitis; sometimes they are due to complications. The more continuous fever, which is common late in the disease, is usually due to tuberculosis—of the peritoneum, lungs, etc.

**Physical Signs.**—The general aspect is often quite characteristic and may suggest the diagnosis. In the early stages there is pallor and sallowness; the face is peculiarly muddy or subicteroid. Later, the patient becomes thin and emaciated; the musculature is soft and flabby; the general integument is dry, harsh, and wrinkled; the face is drawn, occasionally bloated; the eyes are sunken; the conjunctivæ are muddy or subicteric; the cheeks and temples are hollow; the lips are dry and fissured; the tongue is flabby and coated; the gums are spongy and bleed readily; the breath is foul; the skin of the face and cheeks reveals many distended venules that are prone to bleed; nævi consisting of localized stellate varices and so-called mat nævi ("areas of skin of a reddish or purplish color due to the uniform distension of small venules," Osler) may occur on the face, neck, and back; and small capillary, subcutaneous hemorrhages are prone to develop, especially in regions exposed to traumatism. The abdomen is more or less markedly, sometimes enormously, distended, and is in notable contrast to the emaciated face and extremities. The umbilicus becomes everted and has been known to rupture. The abdominal wall reveals enlarged and varicose veins due to the establishment of a collateral circulation. The very obvious communication sometimes established between the superficial epigastric veins and the long thoracic and the mammary veins is due not to the portal obstruction but to interference with the circulation in the inferior vena cava, the consequence of increased intra-abdominal pressure caused, as a rule, by the ascites. The collateral circulation, although

<sup>1</sup> *Internat. Beitr. z. inner. Med.*, Berl., 1902, i, 457.

often marked, is rarely ample or efficient; sometimes it is apparently for a time, at least, since an extensive collateral circulation occasionally relieves more or less permanently a previous ascites, but under these circumstances one cannot ignore the likelihood of the liver having become more pervious to the passage of the portal blood.

Examination shows the *liver* to be enlarged in most cases, but the size varies considerably in different cases and in the same case at different times. Foxwell has well said that the liver is "enlarged at all stages of the disease, and that whether enlarged or contracted the clinical symptoms and course are much the same," a statement that has been especially emphasized by Dreschfeld, Rolleston, etc. Usually before the onset of the ascites, and often during the prevalence of the ascites, the lower border of the liver is palpable one, two, or three fingerbreadths below the margin of the ribs in the right nipple line. The liver is often tender, its edge sharp, and its surface irregular; in some emaciated subjects the hobnail surface can be readily appreciated by the palpating hand, but one must be careful not to confuse therewith irregular areas of fat and fibrous tissue in the abdominal wall. In some cases late in the course of the disease percussion and palpation show the liver to be considerably reduced in size, but in many cases in which the liver appears to be small it is of normal or increased size and elevated, being pushed up by ascites or drawn up by a paretic diaphragm (due to perihepatitis, etc.); in other cases emphysema may decrease the extent of liver dullness, or adhesions may prevent the descent of the organ on deep inspiration. In any event, whether small or only elevated, the organ can often but not always be palpated by firm pressure upward under the ribs. The left lobe is often disproportionately small and not at all palpable in the epigastrium—which is quite significant of cirrhosis. Notable variations in the size of the liver occur from time to time, and often rather rapidly; the common change consists of the reduction in size of a large liver, but the reverse is not unknown, although it may be temporary.

The *spleen* is usually palpable two or three fingerbreadths below the left costal margin; but as also in the case of the liver, tympanites and ascites often interfere with satisfactory examination. Early the spleen is sometimes not notably increased in consistency; later it is usually firm, and it is often tender. It is often much reduced in size by copious gastro-intestinal hemorrhage, severe diarrhoea, the recurrence of ascites after tapping, etc. On the contrary, an unusual enlargement is sometimes a forerunner of hemorrhage, which may be prevented by a prompt resort to free purgation.

*Ascites* is often the first obtrusive manifestation that leads the patient to seek medical advice. Sometimes it is attributed to a definite exciting cause, such as exposure, cold, trauma, etc.; but, as a rule, the onset is gradual and without definite cause, and the accumulation is slow. Occasionally the fluid accumulates with marked rapidity, in which event it is attributable to thrombosis of the portal vein. Ascites is to be looked upon as a late event, although it is not improbable that congestion and transudation of a small amount of fluid into the peritoneum occurs comparatively early, in some cases at least; but this is more or less readily

absorbed. It is present in almost if not quite all subjects dying of cirrhosis *per se*, but in scarcely more than 50 per cent. of cirrhotic subjects at the necropsy table. Klopstock found ascites in 172 of 250 cases of cirrhosis that came to necropsy. There is no direct relationship between the size of the liver and the onset or the degree of ascites; in most cases the liver is larger than normal at the time of development of the ascites; but a large liver may be present without ascites; a small liver is rarely found without ascites. It is believed by many observers, such as Hale White, Rolleston, etc., that ascites is really a terminal event, and that if, in a case presumed to be cirrhosis of the liver, the patient lives to require a second tapping, the cirrhosis is complicated with chronic peritonitis (perihepatitis), or the diagnosis is incorrect.

Some patients require repeated tapings. Casati reports one in whom tapping was done 111 times, and Rumpf a case in which it was done 301 times; but these are most unusual. Usually the tapping is of temporary benefit, relieving the patient's distress for a short time only; the fluid soon reaccumulates, slowly, as a rule, occasionally rapidly. In unusual cases more or less permanent benefit seems to result, doubtless in consequence of the formation of adhesions. Cheadle reports a case in which a man was tapped 19 times and lived eight years after the last tapping; and MacDonald reports two cases in which disappearance of the ascites ensued upon 31 and 60 tapings, respectively.

The *ascitic fluid* varies in amount—in the average case from 4 to 8 or 10 liters, but it may be as much as 20 liters, with consequent enormous distension. The fluid is usually pale amber in color, clear, somewhat opalescent, and alkaline; it has a specific gravity of 1.008 to 1.015, and it contains 0.5 to 1 per cent. of albumin, and occasionally also traces of urea, urobilin, purin bodies, sugar, etc. Sometimes it is turbid from associated peritonitis, in which event it is of higher specific gravity and contains more albumin; rarely it is chylous, chyloform, or hemorrhagic—the last mentioned usually the consequence of traumatism, or petechial hemorrhages in the serosa, etc. Bacteriological examination shows the fluid to be sterile, unless there has been secondary infection. Cytological studies show the cellular constituents to be few and to consist of lymphocytes and endothelial cells, with a few erythrocytes and leukocytes. Cryoscopy reveals the freezing-point to vary with the amount of albumin.

Varying with the amount of fluid there is more or less displacement and compression of the abdominal and thoracic organs. The liver and the diaphragm are pushed upward and cause embarrassment of the respiration and the heart action, and not infrequently compression and consequent congestion and collapse, and perhaps bronchopneumonia, in the bases of lungs, particularly the right.

The ascites is doubtless due to different factors: portal obstruction, peritonitis (or perihepatitis), and toxemia—which are variously operative in different cases. Portal obstruction is an important, but by no means the sole, factor. Ascites seems a natural consequence of the other manifestations of portal obstruction (hematemesis, collateral circulation, etc.), and it is the conspicuous result of complete portal obstruction,



such as occurs in portal thrombosis. The cause of the increased portal pressure in cirrhosis is not immediately patent, and probably it is not always the same. In some cases thrombosis of at least some of the portal radicles is found upon histological examination—which serves to explain, in part at least, the increased portal pressure, in some but probably few cases. Usually the increased portal pressure is attributed to obstruction of the portal vessels by the newly formed connective tissue, but doubt has been thrown upon this by Kretz and by Herrick,<sup>1</sup> who believes that an important factor in this increased portal pressure is the communication of the arterial pressure to the portal circulation. Lessening of the portal area is probably also of some significance in increasing the portal pressure. That increased portal pressure is not the sole factor in causing ascites is apparent from the fact that it is not always present when the portal pressure is undoubtedly high, as at the time of (or just before) severe gastro-intestinal hemorrhages; in these cases, however, the hemorrhage is often due to factors other than the increased portal pressure, such as inflammation and erosion of vessels; and frequently the peritoneal lymphatics are still active and able to carry away a considerable amount of fluid. Usually the fluid is not inflammatory in nature, but sometimes it is, supporting the view that the ascites is sometimes due in part at least to peritonitis (perihepatitis). In part the ascites may be toxic, an unknown toxin acting as a lymphagogue on the peritoneum; but this is pure hypothesis.

*Edema* is common late in the disease, that is, it comes on after the ascites. It is most marked in the feet and legs, but often involves the trunk, especially the dependent portions; rarely anasarca ensues. The œdema of the lower extremities is referable to interference with the venous flow in the inferior vena cava. Edema of the anterior abdominal wall is sometimes related etiologically to increased pressure in the dilated and tortuous regional veins. Occasionally œdema precedes the development of the ascites, in which event it may be due to one of several factors: it may be toxic, in nature analogous to some of the ascites (hypothesis); it is sometimes due to anemia or to chronic renal or heart disease with dilatation; occasionally it may result from thrombosis of the iliac veins or the inferior vena cava; or it may be due to alcoholic neuritis.

The action of the heart is often impeded by the upward pressure exerted by the ascites. The blood-pressure is usually low, the pulse small and frequently rapid, and the breathing labored. The myocardium is often weak, due to fibroid alterations the consequence of alcoholism, malnutrition, and cachexia. A systolic murmur and other evidences of dilatation may develop. A *venous murmur* is sometimes audible in the epigastrium (dilated veins in the falciform ligament), and sometimes over the spleen. Evidences of cardiac failure are sometimes so marked as to obscure the cirrhosis.

The *blood* shows the changes of secondary anemia. There is no leukocytosis unless there is some associated infection. Late in the disease evidences of considerable toxic disorganization of the blood become

<sup>1</sup> *Jour. Exper. Med.*, 1907, ix, 93.

apparent—hydremlia, œdema, submucous and subcutaneous hemorrhages, and the blood-findings may simulate those of pernicious anemia.

The *urine* is usually diminished in amount, in consequence of deficient absorption of fluid, the large amount of fluid in the peritoneum, pressure exerted on the kidneys, and decreased blood-pressure; the specific gravity and the color are high; sometimes the urine is reddish in color (urobilin, urates); it is highly acid; sometimes it contains albumin (congestion due to failing heart, parenchymatous changes, nephritis); sugar is rarely present; the chlorides are diminished; the urea is reduced; the ammonia is increased (effort to neutralize acid intoxication); indican, albumoses, leucin, tyrosin, and increased volatile fatty acids may be found. Alimentary levulosuria may be detected, and may prove a serviceable sign of hepatic insufficiency; which is true also of urobilinuria and phenoluria. In so-called bronzed diabetes (hemochromatosis) sugar is present in the urine, but it is due not to the associated cirrhosis of the liver, but to fibrotic and other changes in the pancreas.

**Complications.**—The cirrhotic subject is peculiarly susceptible to infections of diverse sorts, both acute and chronic. *Tuberculosis* is the most common (more common in adults than in children) and shows a special predilection for the lungs and the peritoneum. The complication is often overlooked, because unthought of and unsought; it should always be suspected when there is fever otherwise unaccounted for. In some cases the lung involvement is altogether latent; in other cases it gives rise to physical signs sufficient for diagnosis, but no obtrusive symptoms; in a few cases it dominates the clinical picture. Tuberculous peritonitis is very common, and not infrequently determines the fatal issue. It is often overlooked, the ascites naturally being attributed to the cirrhosis; it is suggested by the presence of fever, tenderness and rigidity of the abdominal wall, perhaps increase in the amount of ascites previously stationary (the fluid sometimes becomes hemorrhagic), more rapid course, and more speedy death. The ascites seems to predispose to tuberculous infection, which otherwise is uncommon in adult males. The cirrhosis is undoubtedly the primary disorder in the great majority of cases, but some observers believe that in some cases the tuberculosis of the peritoneum is the primary, the cirrhosis the secondary.

Tuberculous *pleuritis* is not rare, but non-tuberculous pleuritis also occurs. The pleuritis may be primary or secondary to disease of the lungs or the peritoneum; in the latter case the infection doubtless travels through the diaphragm. The pleuritis is usually right-sided, but it may be left-sided or bilateral. Some care is required in diagnosing right-sided pleuritis, since compression of the lung by a large liver or ascites may occasion dulness and other signs simulating pleural effusion; or a localized bronchitis or bronchopneumonia may develop.

Evidences of involvement of the kidneys occur in about half of the cases. In some cases there is only a slight albuminuria, attributable to toxic degeneration of the renal epithelium or passive congestion; in other cases in addition to the albuminuria, which is more marked, there are signs significant of parenchymatous nephritis; in most cases (almost

one-fourth of all cases of cirrhosis) the common manifestations of interstitial nephritis occur.

Peripheral alcoholic *neuritis* (neuromuscular pains and tenderness, muscular cramps, cutaneous hyperesthesia, lost knee-jerks, etc.) occurs in a considerable proportion of cases, and is often overlooked or the symptoms are misinterpreted. A number of acute infections, especially pyococcal infections (local and general), endocarditis, croupous pneumonia, etc., are not uncommon, and may determine the fatal issue.

**Diagnosis.**—This is not always an easy matter in the early stages, but it should be made more frequently than it is. In an alcoholic subject with dyspepsia, an enlarged and tender liver suggests the diagnosis; and this is virtually confirmed if to these there be added an enlarged spleen, perhaps recurring attacks of pain in the region of the liver with slight fever or slight jaundice, and urobilinuria. If the diagnosis were made upon these symptoms and the patient treated accordingly, many subjects doubtless would not later exhibit the typical phenomena of advanced cirrhosis; in some perhaps the diagnosis would be incorrect, but in many the disease would be arrested—of the possibility of which the lesions in the hepatic parenchyma afford abundant testimony. Later, when hematemesis, ascites, the hepatic facies, etc., have appeared, the diagnosis can be no longer in doubt.

Little difficulty is likely to be experienced in differentiating *biliary cirrhosis*, which, aside from its rarity, occurs in younger, usually non-alcoholic subjects, and is characterized by persistent jaundice, an enlarged, smooth liver, much enlarged spleen, the absence of all signs of obstruction of the portal circulation, and a very chronic course.

When the liver is enlarged and there is no ascites, one must exclude other causes of enlargement of the liver, such as passive congestion (chronic cardiac or pulmonary disease, cyanosis, usually marked enlargement and tenderness of the liver, some jaundice, urinary signs of congestion of the kidneys, etc.); fatty liver (rather soft and smooth liver, causes of fatty disease of the liver, such as tuberculosis, etc.); amyloid disease (causes of amyloid disease, involvement of other organs, spleen, kidneys, etc.); leukemia (examination of the blood, etc.); malaria (history of chronic malaria or repeated acute attacks, plasmodia or pigment in the blood, disproportionate enlargement of the spleen, irregular fever, cachexia, anemia, response to quinine, and perhaps absence of a history of alcoholism). Syphilis is suggested by a history or other evidences of syphilitic infection, more local distress and pain due to the more marked perihepatitis, irregular enlargement of the liver especially of the left lobe, and more common jaundice; in some cases the diagnosis is impossible and recourse should be had to antisiphilitic treatment.

The occurrence of hematemesis and other gastro-intestinal hemorrhages necessitates differentiation from gastric and duodenal *ulcer*. This is often difficult, but cirrhosis is suggested by a history of alcoholism, enlarged and tender liver, an enlarged spleen, absence of marked evidence of hyperchlorhydria (hyperchlorhydria may occur in cirrhosis), absence of localized epigastric tenderness, etc. In some cases of cirrhosis the hemorrhage is due to associated gastric or intestinal ulceration, which, however, is commonly not of the peptic variety. Hematemesis, especially



if small in amount, may also suggest *carcinoma* of the stomach; but in cirrhosis there are no signs of pyloric obstruction or the evidence of carcinoma afforded by the gastric contents and a tumor is not palpable; indeed, in cirrhosis there is more likely a void in the epigastrium rather than a sense of increased resistance. In the event of gastric carcinoma signs of involvement of the liver are likely to supervene sooner or later, so that ultimately the differential diagnosis has to be made between cirrhosis and secondary carcinoma of the liver; alcoholism, long-continued dyspepsia, and enlargement of the spleen are much in favor of cirrhosis. Should the primary growth be elsewhere than in the stomach, there may be localizing signs or symptoms, and perhaps metastases elsewhere, as in supraclavicular or other glands, etc. Splenic anemia, or Banti's disease, may be excluded by the primary enlargement of the spleen, the early anemia, the later development of signs of portal obstruction, and the comparative youth of the subjects—twentieth to the fortieth year.

When ascites has developed one must exclude other causes of ascites, especially chronic peritonitis and perihepatitis (multiple serositis), thrombosis of the portal vein, tumors of the peritoneum and the abdominal organs, chronic cardiac disease, and cachectic states. As already stated, the ascites in many cases of cirrhosis is due, in part at least, to peritonitis or perihepatitis, but in other cases it may be due solely to perihepatitis, occurring alone or as part of multiple serositis, or in tuberculous peritonitis. *Tuberculous peritonitis* is suggested by the absence of a history of alcoholism and of evidences of portal obstruction, and by the presence of fever, tenderness and rigidity of the abdominal muscles; should the tuberculous peritonitis be secondary to cirrhosis with ascites, there may be rather sudden increase in a previously stationary ascites, a more rapid course, and speedy death.

*Thrombosis of the portal vein* occurs in one-third of the cases of cirrhosis, and is suggested by sudden development of ascites (or sudden increase in the ascites, if already present), rapid enlargement of the spleen, severe (perhaps repeated) hematemesis, and rapid recurrence of the ascites after removal; the sudden onset of these symptoms in the absence of a history of alcoholism suggests primary thrombosis of the portal vein, but in many cases of supposed primary thrombosis there has been a latent cirrhosis until this event.

In the ascites of *tumors* of the peritoneum or the abdominal viscera, the seat of the primary growth may be more or less obvious, metastases may be found in the supraclavicular fossa, in glands, about the umbilicus, along the course of the falciform ligament of the liver, etc.; emaciation and cachexia are more marked than in cirrhosis, and signs of portal obstruction are wanting; should the liver or biliary ducts be involved, there is also deep jaundice and nodular and progressive enlargement of the liver. The ascites of chronic cardiac disease is recognized by detecting the disorder of the heart or an antecedent pulmonary disorder with consecutive hypertrophy and dilatation of the heart; the œdema of heart disease begins usually in the legs and other dependent portions of the body (only exceptionally giving rise to primary ascites); and the œdema and ascites, as well as the size of the liver, vary with the functional activity of the heart, responding, therefore, to cardiac tonics.

The ascites of cachectic states, such as advanced nephritis, amyloid disease, leukemia, various anemic conditions, convalescence from typhoid and other infections, is usually slight in grade, often only part of the general anasarca, and is associated with readily recognizable disorders; only when there is associated cardiac or hepatic disease does the ascites become at all marked.

In some cases of ascites the liver is small—in which event the disorder may be syphilis of the liver, advanced passive congestion (red atrophy), chronic deforming peritonitis and perihepatitis, thrombosis of the portal vein, etc. Each of these should be readily differentiated. The small size of the liver may also be due to acute yellow atrophy superadded to cirrhosis of the liver—which also should be readily recognized.

*Examination of the fluid* removed by tapping (or otherwise) aids in the differential diagnosis. The transudate of cachectic states is clear, pale-amber colored, and limpid; it has a specific gravity of 1.010 or less, and contains less than 1 per cent. of albumin; its cellular content is slight and consists of a few lymphocytes and endothelial cells, and perhaps an occasional erythrocyte. The transudate due to mechanical obstruction is clear-amber colored; it has a specific gravity of 1.008 to 1.014, and contains from 1 to 3 per cent. of albumin; its cellular content consists of a few lymphocytes and endothelial cells, a few erythrocytes, and an occasional polynuclear leukocyte. The inflammatory exudates may be serous, serofibrinous, purulent, or hemorrhagic in character; even the serous exudates are usually slightly turbid; they have a specific gravity of 1.015 or more, and they contain from 3 to 6 per cent. or more of albumin; their cellular content consists of lymphocytes, polynuclear leukocytes, endothelial cells, and erythrocytes in varying proportion, depending upon the nature of the infection; lymphocytes in large numbers (upward of 90 per cent.) indicating tuberculous infection, disproportionate polynuclear leukocytosis indicating pyococcic infection. In tuberculous peritonitis and in malignant disease of the peritoneum the fluid is often quite obviously hemorrhagic. The tuberculous nature of the process may be further demonstrated by culture methods, animal inoculations and resort to tuberculin reactions. That the fluid is due to malignant disease may be proved by finding cells with asymmetrical karyokinetic figures. Occasionally the fluid is chylous (admixture with chyle) or chyloform (fatty degeneration of the endothelial and other cells). These figures relating to the specific gravity and the percentage of albumin of the ascitic fluid are often modified by the occurrence in the one patient of two or more conditions that give rise to ascites.

**Special Types.**—Certain special types of portal cirrhosis may be differentiated, of which the following are the more important: (1) Cirrhosis of hemochromatosis; (2) malarial cirrhosis; (3) anthracotic cirrhosis; and (4) cirrhosis in children.

**CIRRHOSIS OF HEMOCHROMATOSIS (OR BRONZED DIABETES).**—This is a rare disease. Fitcher,<sup>1</sup> in 1907, was able to find references to only 35 undoubted cases, and Potter and Milne<sup>2</sup> in 1912 collected 51 cases. The

<sup>1</sup> *Am. Jour. Med. Sc.*, 1907, cxxxiii, 78.

<sup>2</sup> *Ibid.*, 1912, cxliii, 46.

disorder is most common in men (33 of 35 cases) between the ages of thirty and sixty-one years, but it is most common during the fifth decade. Its characteristics are pigmentation of the viscera and usually also of the skin, cirrhosis of the liver, and fibrosis of the pancreas with involvement of the islands of Langerhans and consequent diabetes. The pigments become deposited in the tissues; the visceral pigmentation antedates that of the skin. The liver, as a rule, is most markedly affected. Mallory<sup>1</sup> believes that the liver cells containing the pigment become necrotic and that leukocytes take up the pigment and damage the connective tissues mechanically by collecting in the lymphatics, thus leading to proliferation of the fibroblasts. In the liver and the pancreas, especially, fibrotic changes develop with the pigmentation and degenerative changes in the parenchyma; in advanced cases these reach a high grade, and in the pancreas ultimately involve the islands of Langerhans and lead to diabetes (but death may ensue before this happens). The sequence of events may be described as hemolysis, chronic interstitial hepatitis and pancreatitis, and diabetes. The liver is usually enlarged and presents the common appearances of portal cirrhosis; it is, however, manifestly pigmented, reddish, resembling brick dust or iron rust. The spleen is enlarged, firm, and pigmented.

The *symptoms* are those of cirrhosis in its early stage, especially the dyspeptic symptoms, and pain in the right hypochondrium; usually also there is progressive weakness. Occasionally the onset may be sudden. The noteworthy signs consist of general cutaneous pigmentation (suggesting Addison's disease), enlargement of the liver and the spleen (quite like that of ordinary portal cirrhosis), and the ultimate development of diabetes. Ascites may be slight or absent; hemorrhages may or may not occur, but death may result from rupture of œsophageal varices, or there may be purpuric attacks. Diabetes when it supervenes is severe; acidosis is common and usually leads to coma.

The *diagnosis* is apparent from the cutaneous pigmentation, enlargement of the liver and the spleen, and diabetes. The cutaneous pigmentation must be differentiated from that of argyria; of chronic jaundice (in which the scleræ are involved); of Addison's disease (in which there is no enlargement of the liver and spleen and no diabetes); and of ochronosis (alkaptonuria).

The *prognosis* is bad, although life may be prolonged for many years. Death may occur suddenly from rupture of œsophageal varices, etc.; usually it occurs within a year after the appearance of glycosuria.

The *treatment* in the early stages is that of cirrhosis; in the later stages, that of diabetes.

**MALARIAL CIRRHOSIS.**—Many observers doubt that malaria ever causes cirrhosis, preferring to believe that the cases of so-called malarial cirrhosis are due to the operation of the ordinary causes of cirrhosis in a malarial subject. It has been suggested that conditions formerly thought to be malarial cirrhosis are the results of the organism of kala-azar. Malarial cirrhosis unquestionably is rare in temperate climates; but in view of the

<sup>1</sup> *Johns Hopkins Hosp. Bull.*, 1911, xxii, 71.



very marked lesions produced in the liver by acute and chronic malaria, especially severe attacks, there can be no well-founded reasons for doubting that malaria may cause cirrhosis.

ANTHRACOTIC CIRRHOSIS is a rare disorder of the liver, described by Welch, and associated with the presence of carbon dust (analogous to coal-miner's lung). Adami has described a similar condition.

CIRRHOSIS IN CHILDREN is by no means rare.<sup>1</sup> Usually it is of the common or portal type; it may be of the biliary type; in congenital syphilis there is a so-called pericellular cirrhosis; and fibrotic lesions sometimes designated cirrhosis are found associated with congenital obliteration of the biliary ducts.

The portal cirrhosis of children is due to the usual causes, such as alcohol, intestinal intoxication, infections, etc. It is not uncommon in several members of the same family, which doubtless is referable to familial habits as regards alcohol, etc., and to the influence of hereditary syphilis (pericellular cirrhosis of the liver), which although cured may leave the liver quite susceptible to the common causes of portal cirrhosis.

The *symptoms* in general conform to those in the adult. Hematemesis is less common (greater distensibility of the spleen in children), diarrhœa and slight jaundice are more common; the liver and the spleen are disproportionately larger than in adults (relative greater volume and more ability for repair in children); tuberculous peritonitis is common and perhaps accounts for most of the ascites and the not uncommon fever.

**Prognosis.**—On the whole, the outlook in portal cirrhosis is not encouraging. There is much evidence that the liver cells early in the disease and often for a long time undergo considerable hyperplasia in an effort to compensate for the damage, and the collateral circulation is additional evidence of efforts in the same direction; there is reason to believe, therefore, that if early recognized and properly treated the disease could often be brought to a standstill, perhaps cured. As a matter of fact, when recognized early, marked benefit is often obtained. The size of the liver is of comparatively little prognostic significance, although a very small liver is indicative of the later stages; as already stated, however, the liver may be enlarged from the beginning to the end. The occurrence of hematemesis does not make the outlook hopeless, since it is sometimes an early symptom and may lead the patient to mend his ways. With the onset of ascites the prognosis becomes distinctly bad, since ascites must be looked upon as a terminal event in the ordinary course of the disease; sometimes, however, the ascites becomes stationary or subsides, in consequence of the establishment of an efficient collateral circulation, and the patient may live for many years. The prognosis is also bad in the event of anasarca, emaciation, cholemia, failure of the heart or the kidneys, and any of the many complications and secondary infections. Ordinarily the disease runs a fatal course within three years from the onset of symptoms; but sometimes arrest ensues and the patient may live for a number of years—eight or ten. Occasionally the course is rapid, six or eight months, especially in young subjects much addicted

<sup>1</sup> Consult Jones, *Brit. Jour. Children's Diseases*, Lond., 1907, iv, 1, 43; and Pexa, *Wien. klin. Rundschau*, 1908, xxii, 33, 50, 68, 83, 117.

to alcohol; in these cases to the cirrhosis is often superadded serious degenerative changes in the hepatic parenchyma, and a form of severe jaundice may ensue and lead to the fatal issue.

**Treatment.**—This to be effective must be instituted during the formative stage; little beneficial effect can be expected after the destruction of much hepatic parenchyma and the overgrowth of much fibrous tissue. The only trustworthy treatment is based upon our conception of the etiological factors, and consists essentially in the avoidance of all causes known or suspected to lead to the disease. Of these, the most important are alcohol, stimulating and highly seasoned foods, foods likely to undergo fermentation in the intestinal tract, etc., all of which must be strictly prohibited. In the early stages, when the hope of marked benefit, if not cure, may be reasonably entertained, alcohol in all forms (including medicinal agents, tinctures, etc.) must be absolutely interdicted; there can be no question that the likelihood of improvement or arrest of the disease depends more upon the non-use of alcohol than upon any or all other factors. But when the disease is well advanced and cure or notable improvement is manifestly impossible, it is not always necessary or wise to discontinue alcohol entirely: the question must be decided for each individual patient. Although it may be quite obvious that the patient's deplorable condition is the consequence of the misuse of alcohol, it does not follow as a corollary that the disuse of alcohol will result in improvement; he may have become so accustomed to the effects of alcohol and so dependent upon it that its withdrawal will be attended by more ill consequences to the general economy than by good results to the liver. In these cases the alcohol should be reduced to the smallest amount consistent with general well-being; and this amount should be given well diluted with the meals. *Nux vomica* or strychnine is often an excellent substitute for alcohol, and is otherwise beneficial; in some cases, after its use for a time, the alcohol may be entirely withdrawn.

The *diet* is of the utmost importance. On the one hand, it must be sufficiently nourishing; on the other hand, it must be absolutely non-irritating to and not overtax the functional capabilities of the liver, and it must be readily assimilable and not likely to undergo fermentation in the intestine, which, if it occurs, may give rise to the production of harmful toxins. Milk is unquestionably the best diet; it is sufficiently nourishing, readily digested and assimilated, its protein is easier utilized by the liver than that of meat; it leaves little residue, and it is somewhat diuretic. In almost all cases it should form the only diet, for a time at least—four to six weeks, depending upon the improvement. Two to three quarts should be given during the twenty-four hours. Sodium bicarbonate or some one of the natural alkaline waters, such as Vichy, Apollinaris, etc., may be added to the milk with advantage; or it may be flavored with vanilla, tea, coffee, chocolate, cocoa, etc. If the milk seems to disagree, skimmed milk, buttermilk, or koumyss (less desirable on account of the contained alcohol) may be tried; in exceptional cases it may be necessary to peptonize the milk. At the end of from four to six weeks in ordinary cases, if improvement has occurred, the diet may be increased by the addition of eggs, gruels, cereals, and stewed fruits,

and from time to time some fish or green vegetables may be permitted. After a month or more, depending upon the condition, the absolute milk diet should be again resorted to for several weeks; thus alternating, the diet should be continued indefinitely. In general, meat, all highly seasoned and stimulating foods, spices, tea and coffee, etc., should be prohibited, because of their irritating effect upon a damaged liver; the use of carbohydrate foods and of fats also should be carefully supervised, since carbohydrates not uncommonly undergo fermentation and lead to the production of toxic substances, and the fats may lead to the formation of fatty acids—all of which may provoke or increase the lesions in the liver. One must individualize, however: in some cases occasional dietetic relaxations are attended by mental as well as bodily satisfaction, a more hopeful outlook, and more or less improvement.

Comparatively little can be done to influence directly the lesions in the liver, but it is always well to try the effect of potassium (or other) iodide, in the hope that it may do good, and with the knowledge that should the lesions be syphilitic benefit assuredly will follow. Minute doses of mercuric bichloride (gr.  $\frac{1}{50}$  to  $\frac{1}{100}$  thrice daily), perhaps combined with the iodide, or ammonium chloride, or nitrohydrochloric acid, also seem to do good in some cases. Rolleston warns against the use of arsenic (which has been recommended to stimulate the hepatic cells to compensatory hyperplasia), believing that it may cause cirrhosis. The use of the alkaline waters or ammonium chloride perhaps retards the development of the terminal acidosis. The use of organic preparations of liver has proved of no value whatever.

Special attention must be paid to the gastro-intestinal tract: indigestion, nausea, vomiting, constipation, diarrhœa, etc., must be prevented as far as possible, and when present should be efficiently treated. In the early stages much benefit may follow a course of treatment at some one of the well-known spas, such as Carlsbad, Vichy, etc. The purgative waters have a good influence in lessening the intestinal catarrh and the portal congestion, and in ridding the system of toxins; their good effect may be as well obtained at home as abroad; or one may give, with the same object in view, sodium sulphate or phosphate, magnesium sulphate, etc., as well as an occasional dose of blue mass or calomel. The good effect of free catharsis is often seen in diminution in the size of the liver and spleen following copious movements. In some cases in which unusual enlargement of the spleen suggests the imminence of hematemesis or other gastro-intestinal hemorrhage, this may be warded off by free catharsis; in other cases ascites may be thus in part absorbed.

The indigestion, nausea, and vomiting are to be treated on general principles; often the disuse of alcohol is followed by immediate improvement in these symptoms; in other cases the additional use of the purgative waters, or saline aperients, is all that is required to secure the desired relief. In other cases, however, medication is required. In one class of cases, sedatives, such as the different preparations of bismuth, creosote, carbolic acid, dilute hydrocyanic acid, silver nitrate, and hyoscyamus



or belladonna, etc., may be desirable; in another class of cases (subacidity) diluted hydrochloric acid, nux vomica, strychnine, and the bitter infusions may lead to the desired result; in still other cases excessive flatulence suggests the use of bismuth, salol, creosote, carbolic acid, and other antifermentatives. Diarrhœa should not be indiscriminately checked, since it may serve a useful purpose of elimination; but when severe and obviously exhausting, it should be met by regulation of the diet and the use of astringents and perhaps small amounts of opium. Pain and distress in the region of the liver may be relieved by hot fomentations or a cold compress locally, abdominal massage, the administration of ammonium chloride, and depletive measures.

*Hematemesis* calls for treatment similar to that of bleeding in gastric ulcer. The patient should remain in bed absolutely at rest, and tranquillity should be promoted by a hypodermic injection of morphine; an ice-bag may be lightly applied to the epigastrium (supported, if necessary); all food and drink should be withheld; to relieve the dryness and thirst the mouth and lips should be moistened, or small bits of ice may be given to the patient to suck, but the water should not be swallowed. Usually in consequence of the quiet and rest thus induced, and of the relief to the congestion afforded by the bleeding, the hemorrhage ceases of itself. If there is much shock and collapse, stimulants and saline infusions should be resorted to. For several days after the hemorrhage no food should be given by the mouth; if deemed necessary rectal enemas may be administered: thirst if distressing, may be relieved by water by the bowel. The subsequent feeding and after-treatment are analogous to those of gastric ulcer.

The onset of severe nervous symptoms (cholemia, acidosis) calls for treatment required in uremia—free purgation, sweating, and diuresis (hot applications to the loins, large amounts of water, alkaline diuretics, digitalis, etc.), and saline infusions. Should diacetic or other acids be present in the urine, large amounts of sodium bicarbonate may be given internally and added to the saline infusion.

*Ascites* may sometimes be favorably influenced by the use of purgatives and diuretics, such as the alkaline diuretics, caffeine, sparteine, theobromine, etc. In the majority of cases medicinal measures are of little if any value in ascites, especially if the amount of fluid be large; resort, therefore, must be had to tapping. This is indicated when the fluid causes local discomfort, dyspnœa, pulmonary congestion, oliguria, etc. There is no advantage in delaying tapping when it has become indicated; indeed, the resort to tapping as often as it may be indicated may lead to the development of adhesions which may augment the already formed collateral circulation. When done under aseptic precautions, the danger of infection may be disregarded; when the fluid is withdrawn slowly there is little likelihood of collapse. The tapping may be done with a trocar and cannula in the median line midway between the umbilicus and the pubes (after preliminary catheterization of the bladder). Continuous drainage is sometimes practised, but does not commend itself. Recently it has been recommended that the fluid removed by aspiration should be

utilized for the purpose of auto-serotherapy, injecting it subcutaneously in small amounts every other day. A small amount of adrenalin has been injected into the abdomen at the completion of a tapping with beneficial results at times.

Operative relief of the ascites and of the conditions upon which it depends is sometimes undertaken. The procedure, which is known as the Talma-Morison operation<sup>1</sup> (omentopexy, epiploexy, Roberts), has for its object relief of the portal circulation, the diversion of the portal blood to the general systemic circulation through the medium of adhesions (and consequent increased vascularity) set up between the liver, the omentum, the parietal peritoneum, etc. How the operation does good has been much discussed. Rolleston points out that the beneficial results cannot be due solely to diversion of the portal blood to the general systemic circulation, since this, imitating an Eck fistula, should tend to provoke or increase toxemia. He suggests that the benefit attained may be due to: (1) Diminution in the flow of blood through the liver, in consequence of which it is enabled to deal more satisfactorily with the blood that does pass through it, and thus reduces the toxemia which is probably an important factor in inducing the ascites; and (2) relief of the venous engorgement and a consequent freer supply of arterial blood consequent upon the vascular adhesions over the surface of the liver, as a result of which the nutrition of the liver cells is improved and they undergo compensatory hyperplasia and become enabled better to perform their function. Of 227 cases collected by Sinclair White, 84 (37 per cent.) resulted in cure and 29 (13 per cent.) in improvement; 34 (15 per cent.) were failures, and death ensued in 75 (33 per cent.). The operation should be done early, while there is hope that sufficient hepatic tissue still remains to discharge reasonable functional demands. The patients submitted to the operation should be carefully selected; associated cardiac, pulmonary, or renal disease, repeated tappings, jaundice, toxemia, and emaciation should be considered contra-indications. Rosenstein<sup>2</sup> has performed the operation known as "Eck's fistula," an artificially formed anastomosis between the portal vein and the inferior vena cava, for the relief of a case of cirrhosis with marked ascites. He reports that the anticipated result was not attained, but that the accumulation of fluid was less rapid than before the operation.

**Biliary Cirrhosis.**—Biliary cirrhosis is a chronic disorder of the liver, probably infectious in origin, characterized anatomically by radicular cholangitis and connective-tissue hyperplasia, and clinically by chronic jaundice and enlargement of the liver and spleen. It is commonly spoken of as Hanot's cirrhosis, hypertrophic biliary cirrhosis with chronic jaundice, in contradistinction to Laennec's, or portal, cirrhosis.

<sup>1</sup> Consult Drummond and Morison, *Brit. Med. Jour.*, 1896, ii, 728; White, *Ibid.*, 1906, ii, 1287 (227 cases); Jones, *Tr. Med. Soc. Lond.*, 1907, xxx, 238; Omi, *Beitr. z. klin. Chir.*, Tübing., 1907, liii, 446 (literature); Lieblein, *Mith. a. d. Grenzgeb. d. Med. u. Chir.*, Jena, 1908, xviii, 794; Koch, *2me Cong. de la soc. internat. de Chir.*, Brussels, September 21–25, 1908, and Grant, *Interstate Med. Jour.*, St. Louis, 1913, xix, 487.

<sup>2</sup> *Archiv. f. klin. Chir.*, Berl., 1912, xlviii, 843.

**Etiology.**—Biliary cirrhosis is especially common during adolescence and early adult life; most cases occur between the twentieth and the thirtieth year; it is rare after the fortieth year, but it is quite common in children (juvenile type), especially in India. In adults about 85 per cent. of the cases (22 of Schachmann's 26 cases) occur in males; in children it is equally common in the two sexes. A seeming hereditary influence is not uncommon; it is mentioned by Osler, Dreschfeld, Finlayson, Rolleston, and others, and it is especially in evidence in the disorder as it occurs in India. Boix, Boinet, and others have pointed out that the disorder may occur in more than one generation of the same family, and that the spleen may be enlarged in certain members of the family who show no evidence of disease of the liver.

The exact nature of the disease is not known. Some, but not all, subjects are alcoholic, and it seems that alcohol plays at most a minor etiological rôle. In the cases so common in children in India it is not in any way an etiological factor. There is some rather inconclusive evidence that the disorder may be the consequence of infection that provokes a radicular cholangitis; but no definite etiological agent has been discovered, nor are the pathways of infection known. That the disorder is an infection is suggested by its sometimes developing after infectious diseases, by the common occurrence of attacks of fever and leukocytosis, and the not rare occurrence of general glandular enlargement. Organisms have been isolated from the blood, liver, and spleen during life in several cases, but the evidence is by no means conclusive that they are related etiologically. The postulated infectious agent is believed by some observers to reach the liver by the general circulation, there being a hemic infection or intoxication of a chronic nature, whence the disease is conceived to be a descending cholangitis; by others the infection is believed to be an ascending infection from the duodenum. The concurrent, sometimes antecedent, enlargement of the spleen and the occasional occurrence of general enlargement of the lymphatic glands are looked upon as evidence of the widespread activity of some infection; the absence or paucity of dyspeptic phenomena and of catarrhal alterations of the duodenum and of the pancreatic duct at necropsy is in favor of the view that the infection does not occur by way of the common bile duct from the duodenum, but by the general circulation. Such evidence as is at hand favors the view that the disease is a radicular cholangitis, the consequence of a general blood infection. It seems likely that the poison does not reach the liver by the portal circulation, since portal toxemia probably always gives rise to the common or portal cirrhosis; but should the postulated microorganisms of biliary cirrhosis produce a poison in the spleen, which is not improbable, this being conveyed to the liver might induce the lesions of portal cirrhosis, which being added to those of biliary cirrhosis might account for some of the cases of so-called mixed types.

**Pathology.**—The liver is enlarged and weighs from 2000 to 4000 grams; its shape is maintained, its consistency increased, and its elasticity diminished. The surface is smooth and exhibits very fine granulations (in marked contrast to the coarse granulations of portal cirrhosis);



adhesions sometimes occur, but are not very common. The liver is usually dark olive green in color. The cut surface is dark greenish or yellowish green in color, smooth, or very slightly granular in advanced cases; usually the liver lobules are more or less obvious, sometimes apparently enlarged, and always separated by widened trabeculae of connective tissue. The gall-bladder and biliary ducts, the hepatic artery and veins, and the portal vein show no abnormalities, as a rule; gall-stones are rarely found, not more frequently than in non-hepatic subjects, which is worth comment in view of the common catarrhal cholangitis which might lead one to expect the formation of bilirubin-calcium calculi.

Microscopically the obtrusive feature consists of an overgrowth of fibrous connective tissue; but the basic and essential process seems to be the radicular cholangitis—which is disclosed by proliferation and desquamation of the epithelium of the small biliary ducts. These lead to obstruction of the lumina of the small ducts, with consequent dilatation of the biliary canaliculi, which in turn are found distended with inspissated bile and bile thrombi (perhaps related to an exudation of inflammatory albuminous fluid). Branching columns of cells, so-called pseudobiliary canaliculi, in and about the periphery of the liver lobules, constitute a conspicuous feature of the lesions. Some of these formations result from proliferation of preëxisting bile ducts; but some of them undoubtedly are derived from proliferation of the liver cells themselves. The liver cells otherwise exhibit comparatively inconsequential changes. The retrograde alterations so common in portal cirrhosis are rare. Apparently for a long time, much longer than in portal cirrhosis, the liver cells are enabled to maintain their structural integrity. Acute necrotic or autolytic changes, however, may occur at any time and determine the fatal issue. The new connective tissue occurs in delicate fibrillar bands that not only course between the lobules but also invade the lobules to a greater or less extent (so-called monolobular, unilobular, or intralobular cirrhosis). In some advanced cases the arrangement of the connective tissue is not so regular, so that it imitates the so-called multilobular or portal cirrhosis. The new connective tissue consists in part of elastic tissue, but proportionately less than in portal cirrhosis.

All the organs of the body are bile-stained. The spleen is enlarged, and commonly weighs from 600 to 1000 to 1500 grams or more; in children it may be as large as or larger than the enlarged liver. It is firmer and denser than normally, and often adherent to the adjacent tissues (perisplenitis). Microscopically it reveals lymphoid and endothelial hyperplasia, and fibrosis with consecutive atrophy of the parenchyma. The pancreas usually shows no noteworthy lesions; occasionally a slight periductal fibrosis has been observed. The gastro-intestinal tract shows no noteworthy lesions, in particular no congestive or catarrhal lesions of the duodenum and the diverticulum of Vater. The lymphatic glands in the portal fissure and usually the adjacent glands are enlarged, œdematous, and congested, but they exert no pressure on the biliary ducts.

**Symptoms.**—The onset is insidious. For a long time there may be ill-defined complaint of poor health, general malaise, weakness, loss of flesh, etc.; or there may be a sense of weight or distress, perhaps actual

pain, in the right hypochondrium; rarely there is some dyspepsia, coated tongue, poor appetite, perhaps nausea, diarrhoea, etc.; in a few cases the patient's attention may be first directed to increase in the size of the abdomen.

In the great majority of cases the obtrusive symptom is jaundice, which is slight at first. The jaundice varies in degree from time to time, but on the whole it tends to increase and eventually it may become extreme, usually greenish; sometimes the markedly bronzed color suggests or is mistaken for that of Addison's disease. The usual concomitants of protracted jaundice are seen. There is often intense itching, sometimes xanthelasma, etc. Bleeding from the nose or the gums or other mucous membranes may occur from time to time for a long period, or there may be recurring attacks of purpura; the urine shows the presence of bile pigment. The feces also contain bile pigments and may be very dark (in contrast to the clay-colored stools of obstructive jaundice).

In addition, the disease is characterized by periodic attacks of more or less severe abdominal pain, especially in the region of the liver, sometimes attended by nausea and vomiting, and associated with fever, leukocytosis, and increase of the jaundice. These attacks occur without regularity and without demonstrable cause, and they last variable periods—several days to several weeks. Usually the fever does not go above 102°; in some cases there is slight fever for long periods. Occasionally these exacerbations are attended by the nervous and other phenomena of icterus gravis, and with high fever, delirium, coma, etc., the patient may die.

The other manifestations are not characteristic. There may be dyspnoea from impeded action of the diaphragm and pressure upon the lungs and the heart by the enlarged liver and spleen. The myocardium may become disorganized, so that dilatation ensues; the pulse is rarely slowed. Diarrhoea is the rule rather than the exception.

*Examination* usually reveals an obvious bulging of the lower right costal arch and the upper part of the abdomen, which is found to be due to a much and uniformly enlarged liver; it may reach, in the right nipple line, from the fourth rib, or higher, to near or below the transverse umbilical line; it occupies a proportionate area in the epigastrium; and it extends well into the left hypochondrium. It presents a smooth surface; rarely it may be slightly irregular from fine granulations on the surface (which, however, are scarcely appreciable by palpation) or from adhesions. The organ is firmer than normal, and its edge is sharp and well defined. Usually the enlargement is progressive, although the size of the organ may vary somewhat from time to time. Rarely toward the end some decrease in size may become apparent (usually more apparent than real), attributed to contraction of the newly formed connective tissue or secondary portal cirrhosis. The liver may be moderately but often is not at all tender. The gall-bladder is not enlarged, except in the event of some complication.

The *spleen* is markedly enlarged, much more so than in portal cirrhosis; it is hard and presents a sharp and well-defined edge. Some writers believe that the enlargement of the spleen may antedate that of the

liver. In children the spleen may be actually larger and heavier than the enlarged liver—the juvenile type of biliary cirrhosis (*cirrhose biliaire splénomégalyque* of Gilbert and Fournier). On auscultation one may sometimes hear a soft murmur or friction (perisplenitis).

The blood reveals oligocythemia, leukocytosis during the periodic exacerbations, diminished coagulability, etc. The urine, usually increased in amount in addition to containing bile pigments, is highly colored and of increased specific gravity; albumin and sugar are usually absent.

Rarely a bulbous enlargement of the terminal phalanges of the fingers (Hippocratic fingers) and of the toes occurs; it is due to thickening of soft tissues (*x-ray* examination shows no bony overgrowth), and although it resembles the hypertrophic pulmonary osteo-arthritis of Marie, it cannot be correlated with any disease of the lungs; presumably, however, it is due to some unknown toxin, which is not peculiar to biliary cirrhosis, since it may be found in other types of protracted jaundice. In children growth is stunted, the condition spoken of as infantilism develops, and the onset of puberty is delayed.

**Types of Biliary Cirrhosis.**—The varying relations between the size of the liver and of the spleen and the time of the onset of these enlargements have led certain French authors, especially Gilbert, Chauffard, Fournier, to postulate different types of the hypertrophic biliary cirrhosis, depending on the priority of involvement of the liver or spleen and also on relative amount of enlargement of these two organs. The differentiations are of minor clinical significance, although they suggest that all cases of biliary cirrhosis are not of the same nature and genesis.

**Diagnosis.**—This, as a rule, presents no unusual difficulties, although it is made more frequently than the rarity of the disease warrants. The important diagnostic features consist of the occurrence in a young, usually non-alcoholic, subject of chronic progressive jaundice, with considerable and persistent enlargement of the liver and spleen, and periodic attacks of abdominal pain, fever, and leukocytosis, with subsequent increase in the jaundice, and no signs of cholelithiasis or portal obstruction.

There should be no difficulty in differentiating the more common or *portal cirrhosis*, which occurs, as a rule, in older and alcoholic subjects and is attended by more marked dyspeptic symptoms and by evidences of portal obstruction. In portal cirrhosis hemorrhages, especially hematemesis, often occur early and are commonly profuse; whereas in biliary cirrhosis hemorrhages are usually a late manifestation and small; they are most common from the oral and nasal mucous membrane and into the skin, and hematemesis is rare. Jaundice sometimes occurs in portal cirrhosis, but it is a complication and catarrhal in nature; in biliary cirrhosis it is the conspicuous feature, and, although permanent, it is not associated with absence of bile from the feces. Constipation is common in portal cirrhosis, diarrhoea in biliary cirrhosis. Portal cirrhosis usually runs a fatal course within three years or less; biliary cirrhosis not uncommonly lasts from five to ten years or more.

The clinical phenomena of biliary and of portal cirrhosis are sometimes combined; that is, jaundice supervenes in a case of portal cirrhosis



with enlarged liver and ascites, or ascites develops in a case of supposed biliary cirrhosis with enlarged liver and jaundice. This has led some authors to believe that biliary cirrhosis is not a disease entity; others postulate mixed forms, or the superaddition of portal cirrhosis to the final stages of biliary cirrhosis. The diagnostic difficulties are much simplified by bearing in mind that biliary cirrhosis is a rare disease; that, although jaundice is not an essential part of portal cirrhosis, it occurs in from 15 to 20 per cent. of the cases, being due to a complicating radicular cholangitis; and that inasmuch as the liver is usually enlarged in portal cirrhosis (although it may become small), an enlarged liver with ascites and jaundice does not necessarily mean a mixed form of cirrhosis, but is quite consistent with the natural history of portal or the common type of cirrhosis. On the other hand, the very rare cases in which ascites supervenes after the long continuance of biliary cirrhosis may be variously interpreted: in some cases the ascites may be due to disease of the peritoneum (perihepatitis, peritonitis, etc.); in other cases it may be due to gross obstruction of the portal vein, or if terminal to cachectic states; in other cases perhaps the lesions of portal cirrhosis are added to those of the primary biliary cirrhosis.

When the jaundice is slight and perhaps readily overlooked, other forms of enlargement of the liver, such as passive congestion, fatty liver, amyloid liver, leukemia, tuberculosis, syphilis, and hemochromatosis must be differentiated. Other causes of chronic jaundice also must be excluded, such as cholelithiasis and carcinoma.

**Prognosis.**—The outlook as to cure is hopeless. The disease usually runs a protracted course, averaging four or five years, but not uncommonly continuing for ten years or more. The periods of remission are often of long duration and the general health may be well maintained; but the exacerbations may be severe and seriously undermine the general resistance, and they may lead to a severe form of jaundice and death. The prognosis is especially bad in the event of severe jaundice with nervous symptoms (fever, delirium, coma, etc.), recurrent hemorrhages, marked general weakness, intercurrent complications, etc.

**Treatment.**—The treatment is largely symptomatic, and in general does not differ materially from that advised in portal cirrhosis. The hygienic conditions should be the best obtainable, and should comprise much fresh air, non-exposure to cold and damp, moderate and carefully regulated exercise, etc. The diet may be more generous than in portal cirrhosis, but with a view not to provoke gastro-intestinal derangements; the patient should avoid dietetic indiscretions, alcohol, etc. Constipation should be overcome by the use of calomel, blue mass, and the salines.

The probable infectious nature of the disorder suggests the use of antiseptics, such as hexamethylenamine and the salicylates, which are eliminated with the bile. Their use has been followed by some apparent improvement. Good results also are reported to have followed drainage of the gall-bladder and biliary ducts; but the diagnosis in some of the cases is open to question: undoubtedly they may have been cases of infection of the biliary tract, but probably not of biliary cirrhosis.

## TUBERCULOSIS, SYPHILIS, AND ACTINOMYCOSIS

These diseases are discussed elsewhere.

## CARCINOMA OF THE LIVER

**Etiology.**—Carcinoma of the liver may be primary or secondary. Primary carcinoma of the liver is a rare disease. Among 11,500 necropsies Hale White<sup>1</sup> found only 11 cases. Secondary carcinoma is more common, the ratio of the primary to the secondary being 1 to 25 (Hale White) or 1 to 40 (Hansemann<sup>2</sup>). Among 4200 necropsies, Hale White found 136 examples of secondary deposits in the liver, of which at least 126 were carcinomatous.

**Pathology.**—Primary carcinoma of the liver appears under three forms: (1) Nodular or multiple carcinoma. This is the most common form, occurring in 65 per cent. (Eggel<sup>3</sup>). (2) Massive carcinoma is the type occurring in 23 per cent. (Eggel). It appears as a whitish or grayish-white opaque mass, often occupying almost if not quite an entire lobe (usually the right). It is sharply defined from the surrounding hepatic tissue, which is compressed and atrophic, and sometimes contains smaller secondary nodules. (3) Infiltrating or diffuse carcinoma is the type occurring in 12 per cent. (Eggel). One or both of the major lobes of the organ become pervaded by new-growth, and often the seat of considerable new fibrous-tissue formation, so that the macroscopic appearances are similar to and are commonly mistaken for portal cirrhosis (the cirrhosis with multiple adenoma, or with carcinoma, of Hanot and Gilbert, and other French authors). Microscopically the cells in carcinoma of the liver are usually polyhedral in type, and are believed to be derived from the hepatic cells; rarely they are columnar in type, and are then referred to proliferation of the epithelium of bile ducts. Transitional types also occur, which suggests the histogenetic equivalence of the liver cells and the cells of the biliary ducts. In some cases the sequence of events is represented by hyperplasia, adenoma, carcinoma. It is doubtful, however, whether the designation carcinoma with cirrhosis is as widely applicable as maintained by French authors—who believe that this represents one-third of the cases of primary carcinoma of the liver. In perhaps the majority of the cases the condition is merely cirrhosis with considerable hyperplasia of the liver cells (nodular cirrhosis); appearances suggesting carcinoma are sometimes due to softening of some of the so-called "hobnails," with rupture into the hepatic or the portal veins, and to thrombosis—either of which may be the antecedent condition.

Secondary carcinoma appears usually as multiple, whitish, grayish-white, or yellowish-white nodules scattered through the organ, most commonly at the periphery, where they often occasion perihepatitis.

<sup>1</sup> *Albutt's System of Medicine*, 1900, iv, 204.

<sup>2</sup> *Berl. klin. Woch.*, 1890, xxvii, 353.

<sup>3</sup> *Beitr. z. path. Anat. u. Physiol.*, Jena, 1901, xxx, 506 (literature).

Often they become umbilicated and softened or hemorrhagic. The adjacent liver tissue is compressed, atrophic, and degenerated.

**Symptoms.**—These are not notably different whether the growth be primary or secondary, although variations occur and, in perhaps one-half of the cases of secondary carcinoma, symptoms referable to the primary growth are not apparent. Usually the onset is insidious; the patient may complain of general ill health, languor, anemia, emaciation, etc., for a long time before the true nature of the disorder is disclosed; in many cases, certainly in at least one-third of the cases of secondary carcinoma, the actual conditions are recognized only at autopsy. In some cases symptoms referable to the primary growth precede, for a variable time, symptoms significant of involvement of the liver; but in a considerable number of cases carcinoma of the stomach, rectum, etc., may be for a long time latent; or the symptoms are not obtrusive, and the first noteworthy manifestations may be referable to the liver. In a small percentage of cases the primary growth remains insignificant; the lesions are most marked in the liver, and the symptoms almost if not exclusively hepatic, consisting of local pain and distress, jaundice, ascites, and enlargement of the liver.

Local discomfort is quite common, but even with large carcinoma there may be no actual pain. The sense of discomfort and weight is usually proportionate to the size and rapidity of growth of the carcinoma; it is often increased by the left lateral posture, which increases the tension on the ligaments. Actual pain sometimes occurs, and may be quite severe, in which event it is attributable to a concomitant perihepatitis; it often radiates to the right shoulder, and may be increased by motion. Sometimes there is more or less local tenderness, especially on deep palpation and occasionally there is severe colicky pain.

*Jaundice* is present in more than half of the cases; it is variable in degree, at first, at least, depending upon its cause, but it tends to increase and become permanent. It may be due to a variety of causes that are often difficult to differentiate. Thus, it is not infrequently due to compression of the common bile duct by a primary growth in the head of the pancreas, or to secondary nodules in the lymphatic glands; it may be due to primary carcinoma of the biliary ducts; or it may be due to pressure on the intrahepatic ducts by sufficiently large nodules, to extension along the lumen of the biliary ducts, or to more widespread obstruction, such as may occur in massive carcinoma. In the last-mentioned instance, if jaundice occurs, which is unusual, it is slight in grade and not associated with clay-colored stools. In the other cases the jaundice is obstructive in origin; it increases in intensity until it becomes of the most severe grade; it is permanent, although for a time, at least, it may vary in intensity; and the stools are clay-colored.

*Ascites* is somewhat less common than jaundice; it occurs in almost if not quite half of the cases; both occur together in about 20 per cent., in which event the ascitic fluid is bile-stained; otherwise the fluid is pale, of low specific gravity, and contains a small amount of albumin; occasionally it is hemorrhagic or chyliform. It varies considerably in amount, but is usually moderate and often for a considerable time



stationary; it rarely requires tapping. Perhaps in some cases the ascites is due to portal obstruction, but this is unusual, since other evidences of portal obstruction are usually absent or in abeyance. In most cases the ascites is due to perihepatitis or peritonitis; in some cases to carcinomatous involvement of the peritoneum.

Progressive enlargement of the liver is the phenomenon that determines the diagnosis. The enlargement may be moderate or very great. Usually it involves the right lobe more than the left, but the percussion dulness is increased in all directions. The liver may be observed to increase notably in size under observation. The edge is usually firm and hard, and it, as well as the palpable surface, is quite irregular—nodular. The nodules vary considerably in size; usually they are firm, especially when small, but as they grow they often soften in the centre and hence become depressed or umbilicated; sometimes this umbilication can be made out by palpation, which is quite diagnostic of carcinoma; in other cases they may seem semifluctuating. Sometimes they suddenly increase in size from hemorrhage; occasionally as they degenerate they become smaller. In the massive carcinoma this nodular formation, of course, does not occur, but one can often make out marked distortion due to a very large new-growth. The gall-bladder can sometimes be palpated as an enlarged pear-shaped tumor at the lower edge of the liver. In a few cases secondary nodules develop along the falciform ligament, and become palpable at or through the linea alba, at the umbilicus; these are conclusive evidence of the real nature of the disorder, but in some cases a microscopic examination of an excised nodule may be required to eliminate tuberculosis.

In many cases the base of the right lung becomes compressed, with dulness and feeble or bronchovesicular breath sounds, etc. In other cases the growth in the liver forms an attachment to and finally penetrates the diaphragm, and sets up pleuritis that may become purulent. In rare cases a nodule in the liver penetrates a branch of the hepatic vein, and the carcinomatous cells, being carried to the lung, set up widespread metastasis. Any of these conditions may be responsible for a harsh, dry cough, but in some cases no abnormalities can be detected to account for the cough, which must be attributed to irritation of the diaphragm (perihepatitis) or the pleura, etc. The liver sometimes merely by reason of its weight, and in other cases by causing kinking, impedes the circulation in the inferior vena cava, and gives rise to dilatation of the superficial veins of the abdomen (but leaves the region of the umbilicus free—which is a point of distinction from the dilatation due to portal obstruction); in other cases œdema of the feet and legs results from this cause, but, especially in advanced cases, this may be due also to anemia, cardiac weakness, thrombosis of the femoral veins or the ascending vena cava, etc. Albuminuria is occasionally observed late in the course and is attributable to anemia and toxic degeneration of the renal epithelium (hepatogenous albuminuria, Tessier); indicanuria and increase of the nitrogenous extractives also may be observed. Hydro-nephrosis may ensue from pressure on the ureter or renal pelvis. Gastro-intestinal symptoms are often present, apart from the cases of primary carcinoma of the stomach; vomiting may result from pyloric obstruction

(pressure or kinking). The spleen may become enlarged, especially in the event of pylethrombosis or carcinoma with cirrhosis.

In the course of time the patient loses strength and emaciates (rarely, when the liver increases rapidly in size and attains huge dimensions, the weight may remain stationary or actually increase); he becomes anemic and cachectic, and phenomena attributed to hepatic insufficiency (cholemia) develop.

**Diagnosis.**—This is not always possible, especially in the cases of secondary growth in which the deposits are few in number, small in size, and deep within the substance of the liver. In another series of cases, in which a primary growth is obvious or found on examination, and in which there is a persisting severe jaundice, cachexia, and a rapidly enlarging and nodular liver, the diagnosis can often be made on inspection alone, especially if the patient be made to take a deep inspiration (whereupon the irregular nodular liver, covered only by a thin layer of skin, will be seen to descend). Between these extremes lie the majority of cases, in which the diagnosis is often difficult. Should the liver seem to be the seat of disease, one must determine (1) whether a new growth is present; (2) whether, if present, it involves the liver, and (3) if so, whether it is primary in the liver.

Difficulty is sometimes experienced in determining whether a new-growth is present, since it may be imitated by fecal accumulation in the colon, and by inflammatory thickenings about the gall-bladder and the biliary ducts. Feces, however, may be indented and pushed about; they change their position spontaneously from time to time, and they may be removed altogether by cathartics and enemas. In inflammatory thickenings about the gall-bladder there is usually a history of past cholecystitis or cholelithiasis; the mass is in the region of the gall-bladder and is single (that is, there are no other nodules on the surface of the liver); the liver may not be enlarged at all, and if so, the enlargement is slight or moderate and uniform; jaundice, if present, varies from time to time, and may clear up altogether (which is practically unknown in carcinoma); and the patient's general health is not so seriously involved.

One must avoid the error of mistaking tumors of adjacent organs for a new growth of the liver. This can usually be done by attention to the symptomatology, a careful physical examination, and by a study of the gastric contents, urine, etc. Tumors of other organs, which are near the liver, may have respiratory movement, but such movement is less common in renal and other retroperitoneal growths, which in addition fill out the loin, are covered in front by the intestine, and do not project so high toward the thorax as hepatic tumors. Tumors of the stomach have a significant symptomatology, often cause dilatation of the stomach, characteristically change the gastric contents, and can usually be found quite separate from the liver. New growths of the omentum, or the thickened indurated omentum of tuberculous or other chronic process, usually has a peculiar elongated or irregular shape and is separated from the liver by a zone of tympany, and the free edge of the liver can usually be felt free and uninvolved.

Should the disorder be definitely located in the liver, one has to eliminate other causes of enlargement, especially cirrhosis, syphilis, abscess, hydatid disease, obstruction of the common duct, as well as other less common disorders, such as passive congestion, constricted liver, leukemia, amyloid disease, fatty liver, etc.

In *portal cirrhosis* there is a history of alcoholism; evidences of portal obstruction are common; the liver usually is uniformly enlarged, although as the disease advances it may grow smaller (in new-growths it continues to increase); the palpable nodules are small, not umbilicated, and not surrounded by intervening areas of smooth liver. *Biliary cirrhosis* occurs, as a rule, earlier in life than carcinoma; the jaundice is early, moderate in grade, and yellowish; since some bile always reaches the intestine, the stools are bile-stained; the liver is uniformly enlarged and smooth; the spleen is enlarged; and the course is less rapid.

In *syphilis* of the liver the pain is often more marked; the liver does not increase so rapidly in size and lessens under the influence of anti-syphilitic treatment; and there is a history or there are signs of syphilis elsewhere. *Abscess* which is sometimes simulated by those cases in which the carcinomatous nodules soften and become semifluctuating, and in which the fever of cachexia, anemia, or terminal infection ensues, may be differentiated by the antecedent disorder, by the absence of cachexia, by the less common occurrence of jaundice and ascites, and by the more common fever, etc.

*Hydatid disease* is much rarer than carcinoma; it develops, as a rule, earlier in life, and is of slower course. The enlargement of the liver is usually single (perhaps double, rarely multiple), smooth, and not tender; the spleen is enlarged; there is seldom jaundice and rarely if ever ascites; and cachexia does not ensue until the disease has lasted a long time.

Having determined the liver to be the seat of carcinoma, it is often difficult, sometimes impossible, to say whether the new growth is primary or secondary. In at least one-third of the cases (in 50 per cent. according to Leube) the primary growth is latent; but in some cases in which it is apparently latent it may be detected upon careful study. Attempts to find it should always be made, since, as already said, secondary growths of the liver are from 25 to 40 times as common as primary growths. The presence of a growth in the liver is presumptive evidence of its secondary nature; this is rendered more likely by the presence of many nodules (which, however, do not exclude a primary liver growth with secondary circumferential nodules); by more marked emaciation; and by the less rapid course and less rapid enlargement of the liver. Primary growths usually are single and cause uniform enlargement of a part of the liver; they less frequently cause jaundice and ascites; and they grow more rapidly and hence lead to less emaciation, but to earlier death.

**Prognosis.**—The diagnosis, of course, brings with it the prognosis: the outlook is hopeless. Hale White gives the duration of life as four months from the development of symptoms in primary carcinoma, and seven months after the development of symptoms referable to the liver in secondary carcinoma.



**Treatment.**—This is purely palliative, and has for its object promotion of the comfort of the patient and relief of his distress. Rare cases have been reported in which a single growth has been removed by operation.

### SARCOMA OF THE LIVER

Sarcoma of the liver may be primary or secondary, but it is very rare.<sup>1</sup> Primary sarcoma may occur as a nodular or a diffuse growth, and may originate from any of the connective tissues of the liver or from the endothelium of the bloodvessels or the lymphatics (angiosarcoma, endothelioma, perithelioma). Secondary sarcoma may follow a primary growth anywhere else in the body, but it is especially common after sarcomas of the bones, adrenal, mediastinum, and uveal tract; the last mentioned are likely to be pigmented. Several years may elapse after enucleation of an eye on account of melanotic sarcoma before recurrence in the liver occurs. Clinically sarcoma cannot be distinguished from carcinoma, except perhaps in the cases that occur in infants,<sup>2</sup> in whom a tumor is more likely to be sarcomatous than carcinomatous. Sarcoma of the liver runs a rapid course, and soon terminates fatally.

### BENIGN TUMORS OF THE LIVER

Benign tumors, such as adenoma, angioma, so-called fibroma, lipoma, etc., are occasionally observed, but are chiefly of pathological interest. Adenomas<sup>3</sup> may be single or multiple, and may develop from the hepatic cells or from the biliary ducts. The biliary-duct adenoma may become the seat of cystic dilatation (cystadenoma or adenocystoma). Another tumor, often described as an adenoma, arises not from liver tissue but from aberrant adrenal in the liver. Multiple adenomas are encountered chiefly in association with cirrhosis (so-called nodular cirrhosis); the adenomatous formations are really localized compensatory hyperplasias of the liver cells. It is difficult, if not impossible, to distinguish between hyperplasia and adenoma: there is no sharp line of demarcation, and both may progress to carcinoma. The single adenoma is not susceptible of clinical recognition unless it becomes very large, when it presents more or less outspokenly the symptoms of carcinoma of the liver. The symptoms of multiple adenoma are those of the basic condition—cirrhosis.

Angioma is a rare tumor, although it is quite as common in the liver as anywhere in the body. They may be congenital or develop in advanced life; they may be single or multiple, and small or very large. They cannot be recognized clinically. Most of the so-called fibromas and lipomas are not true tumors, and one may well doubt whether such tumors occur in the liver.

<sup>1</sup> Consult Marz, *Centralbl. f. allg. Path. u. path. Anat.*, Jena, 1904, xv, 433 (literature).

<sup>2</sup> Consult Pepper, *Am. Jour. Med. Sc.*, 1901, cxxi, 287.

<sup>3</sup> Wätzold, *Beitr. z. path. Anat. u. Physiol.*, Jena, 1906, xxxix, 456 (literature).

### CYSTS OF THE LIVER

Cysts may be parasitic or non-parasitic. The parasitic cysts are due to infection with *Echinococcus granulosus*. Non-parasitic cysts may occur alone or in association with cystic disease of the kidneys or congenital anomalies elsewhere. There may be one or many cysts. According to Moschcowitz the cysts, as a rule, are multiple and most abundant in the zone of the liver just beneath the capsule. They vary in size from those that are microscopic to those that occupy nearly the entire liver. They are equally common in the two sexes, and occur at all ages. They are believed to originate in aberrant bile ducts, in consequence of inflammatory hyperplasia or of retention of fluid the result of congenital obstruction. The diagnosis may be hazarded from the association of an enlarged liver with tumors in the loins (cystic kidneys) or symptoms of chronic interstitial nephritis.

## THE GALL-BLADDER AND BILIARY DUCTS

### ANOMALIES OF FORM AND POSITION

Rarely the gall-bladder may be absent, misplaced, or misshapen. When the gall-bladder is absent, the common bile duct not infrequently presents a circumscribed dilatation (analogue to the gall-bladder); a similar dilatation occasionally develops after operative removal of the gall-bladder. Rarely there is a double gall-bladder with two cystic ducts. Furthermore, the gall-bladder may be misplaced—to the left of the transverse fissure; or it may be embedded more or less deeply in the substance of the liver, and more or less completely surrounded by liver tissue; or the fundus may penetrate the liver substance and present on the anterosuperior surface of the liver. Sometimes it exhibits an hour-glass constriction, aside from the consequences of inflammatory changes. The biliary ducts vary in length. There may be little if any common hepatic duct, due to the unusual length of the right and the left hepatic ducts. The cystic duct may not join the common hepatic duct until close to the insertion into the duodenum. The common bile duct and the pancreatic duct may enter the duodenum separately; sometimes the common bile duct enters with the duct of Santorini. Finally the biliary ducts may be congenitally obliterated.

**Congenital Obliteration of the Biliary Ducts.**—This is a disorder characterized anatomically by obliteration or atresia of the biliary ducts and biliary cirrhosis of the liver, and clinically by persistent jaundice and so-called cholemia which proceed to a fatal issue. The disorder was first prominently brought to the attention of the profession by John Thomson,<sup>1</sup> who, in 1892, collected fifty cases; Lavenson,<sup>2</sup> in 1908, collected sixty-two cases. The nature of the disorder has not been definitely

<sup>1</sup> *Congenital Obliteration of the Bile Ducts*, 1892.

<sup>2</sup> *Jour. Med. Research*, 1908, xviii, 61 (literature)

determined, at least for all cases. It is likely, as stated by Rolleston,<sup>1</sup> that several different conditions may give rise to obstruction or obliteration of the large bile ducts in the new-born, such as peritoneal adhesions set up by fetal peritonitis, syphilis, or a mixed form of hepatic cirrhosis with descending and obliterative cholangitis (the disease usually called congenital obliteration of the bile ducts). Lavenson supported the view that in most instances the obliteration is due to an anomaly of development, and atresia of the ducts, and that the associated cirrhosis is the result of the ensuing biliary stasis.

*Clinically* the disorder is characterized by jaundice, which is present at or develops soon after birth, although rarely it may be delayed for several months; it becomes persistent and intense. The stools become acholic, if not acholic from birth; the urine contains bile pigments; the liver and the spleen are enlarged; vomiting often ensues; and hemorrhages occur from the umbilical cord and into the subcutaneous and the submucous tissues. Gradually the infant emaciates; stupor, coma, or convulsions (cholemia) develop, and death ensues. The course is rarely less than a week; usually it lasts for several weeks or several months. The more benign icterus neonatorum may be distinguished usually by the presence of bile in the feces and by the less-marked jaundice which soon fades. Syphilis may be excluded by the absence of a history of syphilis in a parent, the absence of other evidences of it, non-response to antisyphilitic treatment and by a negative Wassermann reaction.

Rarely a congenital jaundice persists into adolescence or adult life. This type of disorder was first studied attentively by Minkowski,<sup>2</sup> and later by Chauffard<sup>3</sup> who, separating it from the aforementioned types, believes the essential change to be, not a radicular cholangitis, but a splenohemolysis—an anomaly in the destruction of the blood influenced by a primary disorder of the spleen.

### INFECTIONS OF THE BILIARY TRACT

The biliary tract is particularly susceptible to, and frequently the seat of, infections. The result of these varies with the virulence of the infecting microorganism and the resistance offered by the subject: they may be insidious or frank in onset, acute, subacute, or chronic in course, and slight or extremely severe in character; or they may be entirely latent. The frank acute cholangitis and cholecystitis are usually so obtrusive as scarcely to escape recognition; when, however, the infection is more insidious in onset and subacute or chronic, and the infecting microorganisms of low virulence, the resulting lesions are of such nature and the symptoms so slight, or altogether absent, that they are often ill understood, misinterpreted, and referred to other organs.

The introduction of microorganisms of low virulence into the biliary tract may be unattended by pathological lesions; this is the more likely if the ducts are patent and the flow of bile unobstructed. Comparatively

<sup>1</sup> *Brit. Med. Jour.*, Lond., 1907, ii, 947.

<sup>2</sup> *Verhandl. d. XVIII Cong. f. innere Med.*, Wiesb., 1900, p. 316.

<sup>3</sup> *Semaine méd.*, Par., 1907, xxvii, 25.



virulent microorganisms also may be disposed of if the biliary drainage is free and unimpeded, but usually serious and even fatal forms of disease are thus provoked—suppurative cholangitis and suppurative and gangrenous cholecystitis. Between the extremes of mild and more or less innocuous lesions and the severe lesions that lead to quick and early disaster lie the great majority of cases of biliary infection.

The immediate results of moderate or low-grade infection of the biliary tract is the production of a catarrh with the usual inflammatory phenomena—oedema and congestion of the mucous membrane, increased production of mucus, and desquamation of epithelium. If the biliary circulation is free, the results of this catarrh are washed away for the most part, but on account of special local conditions (largely dynamic) they are likely to accumulate, to become accentuated, and to persist in the gall-bladder; in the event of obstruction to the free flow of bile, these are all the more certain to occur. In many cases the lesions thus provoked are entirely latent or without noteworthy symptoms; they may pursue a short course or continue for years; and they constitute the important factor in the etiology of gall-stones.

The inflammatory disorders of the biliary tract, cholangitis, cholecystitis, and cholelithiasis, thus represent varying manifestations of infection; etiologically, anatomically, and clinically they have much in common; and they occur in varying relationships the one to the others—singly or combined. It is important to bear in mind that the one infectious agent, the typhoid bacillus, for instance, may give rise to cholangitis, cholecystitis, and cholelithiasis concurrently or sequentially; that one of these disorders, cholecystitis, for instance, having developed, may lead to another (cholelithiasis), and that the secondary condition serves to maintain the first; that acute catarrhal cholangitis may become chronic and is usually associated with gallstones, and that the one or other of these conditions may lead to suppuration within the biliary tract; that it is often difficult clinically to differentiate these disorders; and that the diagnosis must often comprise more than one of them.

**The Infectious Agents.**—Although considerable interest attaches to postmortem studies of the bacteriology of infections of the biliary tract, the results are frequently vitiated by more or less obvious factors, and they cannot be relied upon implicitly unless the examinations are undertaken within a very short time after death. The conditions at operation are quite different and the results much more trustworthy—although in subsiding or long-standing infections the primary infective agent may not be recovered, since it may have died out or have become overgrown by secondary invaders. At the German Hospital, Philadelphia, Kelly studied the bacterial cause of the infection of the biliary tract in 240 of the patients operated upon by John B. Deaver:

	Cases.	Per cent.
Bacillus coli communis was found in . . . . .	68	28.33
Bacillus typhosus was found in . . . . .	27	11.25
Staphylococcus pyogenes aureus was found in . . . . .	7	2.92
Streptococcus pyogenes was found in . . . . .	1	.42
Staphylococcus pyogenes albus was found in . . . . .	2	.83
Bacillus coli and Staphylococcus aureus were found in . . . . .	2	.83
Unidentified bacilli were found in . . . . .	6	2.50
The cultures remained sterile in . . . . .	127	52.92

In general these results do not differ materially from those obtained by other observers. Other bacteria, however, have been isolated from the biliary tract, such as the cholera bacillus, *Bacillus subtilis*, *Bacillus capsulatus aërogenes*, leptothrix, etc. Biliary infections complicating pneumonia and influenza suggest the possibility of the pneumococcus and the influenza bacillus respectively being the etiological agent. Some etiological importance attaches to anaërobic bacteria—which abound in the intestine. A most suggestive study of this entire question has been published by Lippmann.<sup>1</sup>

**The Pathways of Infection.**—These are: (1) The diverticulum of Vater and the common bile duct; (2) the portal circulation; (3) the systemic circulation; (4) the lymphatic circulation; and (5) directly through the wall of the gall-bladder or the biliary ducts from the peritoneum.

1. *Infection from the duodenum by way of the diverticulum of Vater and the common bile duct* has long been looked upon as at once the most likely and the most common source of biliary infections, but whether with good reason remains to be decided. Although the frequency of *Bacillus coli communis* and of *Bacillus typhosus* in infections of the biliary tract suggests an intestinal source, these bacteria find a direct pathway from the intestine to the liver by the portal circulation. Furthermore, whereas the jejunum and the ileum always contain many bacteria, the duodenum when free from food is often bacteria-free; certainly, in health its bacterial content is small and it does not contain the bacteria often found in cholangitis, cholecystitis, etc. It is quite conceivable, however, indeed it is quite likely, that in conditions of disease of the upper intestine, when bacteria are present in the duodenum, the biliary tract may become infected by way of the diverticulum of Vater; doubtless many of the cases of so-called catarrhal jaundice following gastroduodenitis arise in this fashion. But there are at least two important factors opposing a ready ascending infection of the biliary tract: the one, the action of the sphincter of the diverticulum, which has been estimated by Oggi<sup>2</sup> as exerting a force equal to a pressure within the common bile duct of 700 mm. of water; the second, the influence of the free flow of bile. Indeed, it is doubtful whether infection of the biliary tract ever takes place by way of the diverticulum of Vater in the absence of stasis of the bile. One of the most important factors in preventing such infection is the free flow, that is, the regular periodic expulsion, of the bile—the free flow of the bile rather than the bile itself, since the bile is a quite favorable medium for the growth of bacteria.

2. *Infection by way of the portal circulation* is a common source of biliary infection. Definite experimental proof that the bile may become infected from the circulation was furnished years ago by Blachstein<sup>3</sup> and Welch,<sup>4</sup> and their results have been amply confirmed and amplified, so that there is no doubt that bacteria transported to the liver by the portal circulation may be found in the bile. Under normal circumstances bacteria carried to the liver by the portal circulation are there destroyed

<sup>1</sup> *Le microbisme biliaire normal et pathologique*, Paris, 1904.

<sup>2</sup> Quoted by Naunyn, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, Jena, 1905, xiv, 537.

<sup>3</sup> *Johns Hopkins Hosp. Bull.*, 1891, ii, 96.

<sup>4</sup> *Ibid.*, 121.

by the bactericidal properties of the liver cells; but there is a limit which when overcome permits the entrance of bacteria into the biliary passages. Adami having shown that under apparently normal conditions bacteria may be found in the deeper layers of the intestine, in the portal circulation, and in the liver, suggests that they invade the portal circulation through the aid of the leukocytes—which are especially active during digestion, carrying foodstuffs, foreign matters, bacteria, etc., between the epithelial cells to the lymphatic radicles and the portal venules. Ordinarily most of the bacteria are destroyed; sometimes, however, they pass through the liver and appear in the bile; in other cases they invade the general circulation. This is the latent infection of Adami and certain French and German writers.

3. *Infection by way of the systemic circulation* is probably not an exceedingly common source of infection of the biliary tract. Its importance has been enhanced since we have ascertained the frequency of bacteremia in the great majority of infectious processes. Doerr found that micro-organisms injected into the general circulation of rabbits appear in the gall-bladder within a few hours, and that typhoid bacilli and colon bacilli multiply in the gall-bladder and may be recovered therefrom in pure culture even after four months. The occurrence of cholecystitis and cholangitis as a complication of general infections, such as influenza, pneumonia, etc., also suggests the likelihood of the infection occurring by way of the general circulation; but one must concede the possibility of the local biliary infection being due to organisms other than those occasioning the primary infection, and that the complicating infection may occur by way of the portal circulation or the diverticulum of Vater. Infection by the hepatic artery is a descending infection and operates as does infection carried by the portal circulation—since both circulations commingle at the periphery of the liver lobules; but infected blood carried by the cystic artery may, although probably rarely, lead directly to infection of the gall-bladder without the intermediation of infected bile.

4. *Infection by way of the lymphatic circulation* is probably a most infrequent source of infection.

5. *Direct infection through the wall of the gall-bladder* or of the ducts from the peritoneum has been suggested as a possibility; but excluding cases of general peritonitis in which the gall-bladder may participate secondarily and in which the mechanism of the local infection may be quite obvious, it is doubtful if infection of the biliary tract directly from the peritoneum can occur in the absence of adhesions—in which event it is probably an infection by way of the lymphatic circulation.

The pathways of biliary infection vary with the infecting agent. *Bacillus coli* infections, which must be looked upon as the most common, doubtless occur most frequently by way of the portal circulation. In most cases the liver in full functional activity is enabled to destroy or render innocuous such colon bacilli as may pass the barrier of the intestinal mucosa and be transported to it; but should the physiological activity of the liver become impaired, or should the colon bacilli become of heightened virulence, bacilli of attenuated virulence may pass over into the biliary circulation and, being excreted with the bile, set up a



low-grade biliary catarrh. This commonly passes unnoticed but it is one of the most important factors in the etiology of gall-stones, as it is also the most important factor in the complications of gall-stones. We must admit that in the event of gastro-duodenitis colon bacilli may infect the biliary passages by way of the diverticulum of Vater and the common duct; in this event, the lesions are likely to be more abrupt in onset and more manifest clinically.

### ACUTE CATARRHAL CHOLANGEITIS (CATARRHAL JAUNDICE)

**Etiology.**—Acute catarrhal cholangitis, more commonly called catarrhal jaundice, is a common disorder in young adults, although it occurs at all ages; it is more common in men than in women, largely because of men being more under the influence of the exciting causes. The disorder usually follows in the wake of gastro-intestinal catarrh. Perhaps most cases follow some dietetic indiscretion or overindulgence in alcohol. These set up gastro-intestinal catarrh, which spreads to the biliary papilla and causes swelling of the mucosa and obstruction to the free flow of bile.

Jaundice is an occasional accompaniment of certain infectious diseases, such as typhoid fever, pneumonia, etc. In some cases it results from spread to the biliary papilla of gastro-intestinal catarrh, that is, the jaundice is obstructive. It seems impossible to distinguish clinically between all cases of mild jaundice; some are catarrhal, some toxic, whereas in others, catarrhal in the beginning, the infection may travel up the ducts and involve the finer intrahepatic radicles. Catarrhal jaundice may be due also to passive congestion of the duodenum and swelling of the mucosa; thus it occurs in portal cirrhosis, in advanced stages of cardiac disease, etc.; but the jaundice of portal cirrhosis may also be due to radicular cholangitis, and that occurring in advanced heart disease to pressure exerted on the biliary radicles. Catarrhal jaundice also may complicate organic diseases of the liver, but the jaundice that occurs in syphilis, carcinoma, hydatid cyst, etc., is more commonly due to pressure on the ducts from without than to catarrh. In some cases of supposed catarrhal jaundice no adequate cause can be determined.

**Pathology.**—The lesions consist of congestion, swelling, œdema, and increased production of mucus at the lower end of the common bile duct and of the duodenal mucosa adjacent to the diverticulum of Vater. In some cases the swelling itself is sufficient to obstruct the flow of bile, but in other cases a plug of inspissated tenacious mucus effectually blocks the diverticulum of Vater. The swelling and congestion often subside after death, so that their absence at the necropsy is not trustworthy evidence of their absence during life. All the tissues are bile-stained; rarely the liver may be swollen; the biliary ducts and perhaps the gall-bladder may be distended from the accumulation of bile.

Opportunities to study the lesions in catarrhal jaundice are rarely afforded, since the disease in itself is not fatal. There are many reasons,

however, for believing that the cases interpreted as catarrhal jaundice are not all of one type. In many cases, doubtless, the lesions are as described; in others, perhaps, the lower end of the common bile duct, itself not diseased, is obstructed from without by catarrhal changes in the surrounding duodenal mucosa; in other cases the swelling and consequent obstruction occur perhaps higher up in the common bile duct, or in the hepatic duct, or involve the finer intrahepatic branches. It is not unlikely that many cases are as that described by Eppinger,<sup>1</sup> who studied the lesions in a case of catarrhal jaundice in which death occurred from accident on the eighth day. The significant lesion was hyperplasia of the lymphoid tissue of the mucosa of that part of the common biliary duct that runs in the wall of the intestine; this led to complete occlusion of the common duct and dilatation of the rest of the biliary system. Eppinger suggests that this lymphoid tissue is analogous to that of the tonsil, and is provided at the end of the biliary ducts as a means of defense against infection from the intestine; that it is subject to attacks analogous to tonsillitis; that epidemics of catarrhal jaundice may be analogous to epidemics of tonsillitis; and that some attacks of jaundice in young persons developing without obvious cause may be due to a so-called lymphatic constitution.

**Symptoms.**—In most cases the early symptoms are those of the provoking gastro-intestinal catarrh: loss of appetite, bad taste in the mouth, coated tongue, foul breath, epigastric distress especially after eating flatulence, nausea, and perhaps vomiting; there may be constipation, or perhaps diarrhœa from extension of the intestinal catarrh; and the patient complains of headache, vertigo, mental depression, general malaise, etc. Rarely there is an acute onset, jaundice being the first symptom noticed; but in most cases after the mentioned symptoms have lasted for a few days to a week, the patient notices, or his attention is directed to the fact, that he is slightly jaundiced. The jaundice is of slow and insidious onset, and gradually increases. It is first and best seen in the sclerotic coats of the eyes; soon the integument of the face becomes discolored, and then that of the rest of the body and the visible mucous membranes. With the appearance of the jaundice, sometimes before there is any obvious jaundice, the stools become pale in color and soon are devoid of bile pigment; the urine becomes scanty, dark in color, deposits an abundant sediment, and shows the presence of bile pigments. Usually the bile pigments can be detected in the urine before the appearance of the jaundice in the sclerotics.

When the disorder is fully developed, that is, at the end of four or five days, the discoloration of the skin and mucous membranes is usually well marked, but even when highly developed the color is distinctly yellow, the dark olive-greenish discoloration of malignant disease never developing. Pruritus is often marked; sometimes it even precedes the development of the jaundice. The itching is sometimes so extreme as to induce severe eczema in consequence of uncontrollable scratching. The pulse usually is slowed, 60 or less per minute, and may reveal the

<sup>1</sup> *Wien. klin. Wchnschr.*, 1908, xxi, 480.

dicrotism of low vascular tension; sometimes this is obvious as a well-marked capillary pulsation. The patient usually is irritable or melancholic, often sleepy, and loses flesh and strength.

In most cases neither the liver nor the gall-bladder is palpably enlarged or tender; sometimes, however, the liver can be felt below the costal margin. In cases in which the liver or gall-bladder is much enlarged one should suspect a complicating cholecystitis or inflammation of the intrahepatic ducts. The spleen may be enlarged. Fever (101°) is occasionally present, but it is rarely due directly to the cholangitis, except in the epidemic infectious cases; that which sometimes occurs at the beginning of the attack and lasts a day or two is probably due to the gastro-enteritis; when conspicuous or when it lasts more than several days, it suggests some one of the types of toxic or infectious jaundice (of which, in reality, it may be a mild manifestation). Often late in the disorder the temperature is subnormal.

At the end of about a week, sometimes not until later, the evidences of gastro-intestinal irritation subside, the bad taste in the mouth and the coated tongue disappear, and the appetite returns; in some cases, however, nausea and vomiting persist for ten days or more; and in most cases constipation continues as long as the feces are clay-colored. Gradually the evidences of biliary obstruction lessen, bile pigments appear in the feces, and disappear, first from the urine and then from the skin, where, however, traces may be found for several months. Restoration of the general health is often much delayed; and may not occur until the bile pigments begin to be removed from the tissues. Ordinarily an attack lasts three or four weeks, but sometimes six weeks or more.

**Diagnosis**—In most cases the diagnosis is readily made from the youth of the patient, an antecedent gastro-intestinal catarrh provoked by some more or less obvious cause, and the absence of local pain and of serious involvement of the general health (emaciation, etc.); the diagnosis is further confirmed by the benign and favorable course, which in many cases definitely determines the diagnosis. Doubt regarding its catarrhal nature should always be awakened by the occurrence of jaundice in a middle-aged or elderly person, if it becomes deep or olive-tinted, and if it lasts more than six weeks. Jaundice in a middle-aged or elderly person is much more likely to be due to impaction of a gall-stone, or to carcinoma compressing the common duct. In gall-stones there is usually a history of past infection of the biliary tract, or of definite attacks of cholelithiasis, and the jaundice is commonly preceded by pain; in impaction of the calculus in the common duct there are usually periodic attacks of chills, fever, and sweats, and variation in the degree of the jaundice; occasionally, however, in protracted catarrhal jaundice, fluctuations in the intensity of the jaundice occur, but these relapsing cases are usually referable to repeated dietetic or other indiscretions. Mild grades of so-called toxic or infectious jaundice may be mistaken for catarrhal jaundice—perhaps often they are only different grades of the same process; but in infectious jaundice there is usually an acute onset with fever, and signs of general infection are more prominent—enlarged spleen and liver, albuminuria, etc.



**Prognosis.**—As a rule, the prognosis is good; the disease of itself does not endanger life, and recovery is usually complete and lasting. Most cases last from three to four weeks, but sometimes longer; cases lasting five months and followed by recovery have been reported, but protracted as well as relapsing cases of jaundice are usually due to causes other than catarrh. So-called abortive cases of slight grade and short duration may subside entirely within two weeks or less. In cases that begin with much fever the prognosis at the beginning should be guarded, since they may be the early stage of, and progress to, serious and fatal forms of jaundice. Protracted cases in middle-aged and elderly persons are sometimes of serious import—in consequence of impairment of the general nutrition and the tendency to hemorrhage. Usually complete recovery ensues, but sequels are not unknown; recurrences are not uncommon, especially in those who repeat dietetic and other indiscretions. In some cases a mild grade of chronic catarrh persists, which, involving the gall-bladder and the intrahepatic ducts, may lead to hydrops of the gall-bladder, a mild chronic cholecystitis, cholelithiasis, etc., and perhaps also to some cases of Hanot's biliary cirrhosis; and from progress of the infection, to infection and chronic inflammation of the pancreas.

**Treatment.**—The treatment is essentially that of the gastro-intestinal catarrh, commonly provocative of the cholangitis. The patient should go to bed; for several days at least the diet should be reduced to a minimum, and should consist of a moderate amount of milk, preferably skimmed milk, or broth. The common distaste for food is a good indication to give no food whatever for a day or two, and to be content to relieve the thirst with copious draughts of water, which are usually relished and well borne. The natural alkaline waters are especially serviceable; but alkalis, especially sodium bicarbonate, may be added to ordinary water. Nausea and vomiting, if they persist after withdrawal of the food, may be relieved by lavage with hot alkaline water, the drinking of hot alkaline water, or the administration of bismuth subnitrate or subcarbonate, carbolic acid, etc.; or by warm applications to the epigastrium. The bowels should be opened freely. Custom sanctions the use of calomel, which may be given in a single large dose or in repeated small doses (a blue pill is equally efficacious); it should be followed by a saline aperient. These are much more efficacious if taken hot (or in hot water), in which event they exert an increased beneficial action on the gastro-intestinal catarrh. They should be given in sufficient dose to cause one or two free evacuations daily; more are undesirable. The diarrhœa sometimes present in the early days of the attack rarely demands treatment. Occasionally it may be necessary to administer astringents and antifermentatives, but preparations of opium should be avoided.

After the lapse of several days, when the gastro-intestinal catarrh begins to subside, the tongue to clear, and the appetite to return, additions may be made to the diet, but for some days still, only milk diluted with lime-water or Vichy-water, thin or strained soups, milk toast or dry toast, fish, etc., should be allowed. Later one may add chicken, chops, rice and other carbohydrates, the finer green vegetables, etc.;

but for some time all highly seasoned food and food likely to undergo fermentation must be avoided. The indication of progress toward recovery and of permissible liberality in diet is found not in the degree of jaundice but in the return of bile pigment to the feces and its diminution in the urine. The use of the alkaline aperients should be continued. Injections into the rectum of cold water are sometimes very efficacious in stimulating intestinal, and perhaps also gall-bladder, peristalsis. As the biliary stasis begins to subside, diluted nitrohydrochloric acid and bitter tonics render excellent service. Excessive flatulence is sometimes distressing; it may be relieved by the use of bismuth salicylate, soda-mint, aromatic spirit of ammonia, chloroform water, and antifermentatives.

The pruritus is best relieved by the measures that tend to relieve the biliary catarrh and thus promote the removal of bile pigments from the tissues. Temporary relief may also be obtained by the use of cold sponging, or of a carbolic acid lotion (1 to 40 to 60), or the internal use of the bromides or other nerve sedatives. The general health requires attention for some time, often months, after an attack of catarrhal cholangitis.

### SUPPURATIVE CHOLANGEITIS

**Etiology.**—Suppurative cholangitis results from virulent bacterial infection of the biliary ducts. The common infectious agents are *Bacillus coli communis*, staphylococci, streptococci, pneumococci, *Bacillus typhosus*, the comma bacillus, *Bacillus aërogenes capsulatus*, etc. *Bacillus coli communis* is sometimes found alone, but it is not improbable that in some of the cases it is a secondary invader, or has been present in association with and has outgrown the other or primary infectious agents. *Bacillus aërogenes capsulatus* usually invades the tissues only during or just prior to death, but occasionally it is the primary agent and may be found during life.

The infection may occur by way of the portal or the general systemic circulation (descending infection), or by way of the duodenum and the diverticulum of Vater (ascending infection). Infection sometimes occurs in certain general infections, but it is rendered much easier of accomplishment by local disease of the biliary tract; indeed, in the absence of very virulent infection it is doubtful if infection of the biliary tract ever occurs in the absence of local biliary disease, since the free flow of bile usually is an effective preventive of biliary infection. Suppurative cholangitis, however, is occasionally observed in association with general infections. The provoking microorganism, aside from the typhoid bacillus, is often not that of the primary infection, but the colon bacillus or the pyogenic cocci. This cholangitis rarely occurs without concomitant cholecystitis.

In the great majority of cases suppurative cholangitis is definitely related to local disease of the biliary tract. The local disease acts as the necessary predisposing agent; this comprises all disorders that interfere with the free and unimpeded circulation of the bile and reduce the resistance of the biliary ducts. The commonest antecedents of suppurative

cholangitis are gall-stones and tumors obstructing the ducts. Gall-stones themselves are a consequence of low-grade biliary infection and catarrh, and by the obstruction to the flow of bile that they induce, as well as because of the consequent reduction in the resistance of the biliary mucosa, they participate in the formation of a vicious circle. Suppurative cholangitis thus may supervene upon long-standing chronic catarrhal cholangitis with or without cholelithiasis, upon acute impaction of a gall-stone in the ducts, and upon chronic infective cholangitis with a gall-stone in the common duct (intermittent hepatic fever). Tumors of the biliary ducts or of the adjacent tissues that may obstruct the ducts also favor the development of suppurative cholangitis by obstructing the flow of bile and causing secondary dilatation and reduction in the resistance of the ducts, and, in the event of the growths becoming ulcerated, by affording a means of ready access for bacteria.

**Pathology.**—Although the process may be more or less limited it is usually widespread. The biliary ducts are dilated (in advanced cases often enormously dilated) and filled with purulent material, commonly stained with bile. The walls of the ducts are much thickened, softened, and obviously the seat of purulent infiltration; the mucosa is congested, œdematous, and covered with a layer of mucus, and in fairly well-advanced cases irregularly ulcerated. Usually analogous changes are found in the gall-bladder. About the terminal branches of the biliary ducts there are usually small abscesses; these may be very small and very numerous, but in advanced cases some at least have attained considerable size, in consequence of confluence of several or many small abscesses. The liver is enlarged, swollen, softened, and opaque; the surface usually is irregular, in consequence of the projection of many small abscesses. The cut surface is quite characteristic: more or less, sometimes enormously, dilated biliary ducts, filled with pus (multiple abscesses), with the intervening liver tissue, the seat of marked periductal congestion, parenchymatous degeneration, and necrosis. The abscesses on the surface of the liver may extend to the adjacent peritoneum and set up perihepatitis or more widespread peritonitis, and perhaps extend to the pleura and the lungs or the adjacent intestine; or the process may involve the portal vein, or the hepatic artery; or the suppuration may extend along Wirsung's duct and induce suppurative pancreatitis and abscess in the lesser omentum. The adjacent lymphatic glands, especially those in the portal fissure, are congested, swollen, softened and sometimes necrotic.

**Symptoms.**—The symptoms are not always distinctive; sometimes not even suggestive. Usually there is a history of antecedent cholelithiasis or vague symptoms that may be interpreted as due to gall-stones; in other cases there is some impairment of the general health, which, in the light of subsequent events, may be ascribed to malignant disease; in still other cases the patient suffers from, or has recently suffered from, some general infection, such as typhoid fever, etc. The onset is often insidious; occasionally the first noteworthy symptom is slight jaundice, but in perhaps most cases, especially in cases in which there has been antecedent jaundice due to other causes, the onset is announced by



constitutional phenomena, such as chills, fever, and sweats. These are usually severe, more or less frequently repeated at irregular intervals, and soon lead to considerable impairment of the general nutrition, emaciation, loss of appetite, nausea, perhaps vomiting, diarrhœa, etc.; variable afebrile periods, however, are not uncommon. Jaundice is almost always present, but it is variable in degree; usually it is slight or moderate only, except in cases in which the cholangitis is associated with other conditions that cause intense jaundice. Rare cases of suppurative cholangitis without jaundice have been described.

Sometimes there is no pain in the region of the liver. Usually there is at least dull aching or discomfort (tension of the liver capsule); now and then there is more severe pain due to acute cholecystitis, cholelithiasis, obstruction of the ducts, perihepatitis, peritonitis, etc. The liver is enlarged and usually continues to enlarge. It presents a smooth surface, except in the event of an unusually large abscess presenting on the palpable surface, and it is tender; perhaps, also, there may be a tender spot posteriorly on the right side on a level with and 2 to 3 cm. from the twelfth thoracic vertebra (Boas). Usually the gall-bladder is enlarged and tender (acute cholecystitis). The spleen also may be enlarged. Examination of the blood reveals polynuclear leukocytosis, more marked during and just after the febrile periods; sometimes it is absent during the afebrile periods.

Extension of the lesions locally may lead to the ordinary signs of local or general peritonitis, pleuritis, etc., with perhaps evacuation of pus through a bronchus. Absorption of toxins may induce severe headache, joint pains, swelling, and tenderness, and their excretion may be attended by albuminuria and casts. Involvement of the hepatic vein may lead to multiple abscesses in the lungs, infectious endocarditis, general septicopyemia, etc. Sometimes a single abscess ensues, and may establish communication with the intestine or pleura and lung.

**Diagnosis.**—This is usually apparent from a history of antecedent gall-stones or other disorder of the biliary tract, or of typhoid fever or other infection, and the development of chills, fever, and sweats, and jaundice, local pain, progressive enlargement of the liver, perhaps also of the gall-bladder and spleen, and leukocytosis. In the absence of a history of antecedent disease of the biliary tract, the other symptoms mentioned, if at all outspoken, suffice for the diagnosis; but in many cases the symptoms are added so insidiously to those of the antecedent disease, or they are, in the beginning at least, so mild and evanescent, that it is difficult if not impossible to say just when the suppurative process began or how severe it is. A slight and temporarily increased obstruction to the flow of bile may lead to increased absorption of toxins from a chronically infected biliary tract and increase of the general and local symptoms; release of the obstruction may permit of the free discharge of pus from the biliary tract with subsidence of the symptoms. Thus in some cases recurrences and remissions of the symptoms occur, for instance in the discharge of an impacting gall-stone, drainage may become very free and lead to temporary subsidence of the symptoms.

Difficulty may be experienced in differentiating suppurative pylephlebitis, other forms of abscess (especially solitary or tropical abscess), malaria, etc. Jaundice is not an essential symptom, but it is suggestive of and occurs earlier in suppurative cholangitis than in pylephlebitis or single abscess of the liver. Enlargement of the spleen, while it occurs in suppurative cholangitis and pylephlebitis, is more common in pylephlebitis; but cholangitis and pylephlebitis may coexist. In abscess there is usually a history of antecedent dysentery. Malaria may be excluded by the absence of periodicity of the chills, fever, and sweats, the absence of plasmodia from the blood, and the presence of leukocytosis.

**Prognosis.**—This is decidedly unfavorable, but it is modified by a number of attending phenomena and the treatment. In view of the difficulty of determining accurately the time of onset, it is difficult to say how long it lasts; but the acute cases which pursue a progressive course seldom continue more than three weeks. In less severe cases, in which the infection is less virulent and becomes subacute or chronic, or in which the lesions gradually subside and perhaps become localized to the gall-bladder, or in which a fistulous communication is established with the hollow abdominal viscera or the thoracic viscera, and the pus is discharged, etc., the duration may be much longer and recovery may ensue. The prognosis is materially improved by the spontaneous or operative removal of the source of obstruction (gall-stones, etc.) and the consequent free drainage.

**Treatment.**—Prevention is much more readily effected than cure. Even minor grades of biliary infection, such as the acute and more chronic catarrhal cholangitis (jaundice), gall-stones, etc., should be carefully and persistently treated. This, especially in the event of gall-stones, comprises surgical intervention—which not only is curative of the gall-stones and the accompanying catarrh, but preventive of the more serious suppurative cholangitis. When suppurative cholangitis has developed, the treatment is essentially surgical, and consists in the establishment of free drainage. Medical treatment may be used in conjunction with surgical, and consists in the use of salicylates, hexamethylenamine, and other remedies to disinfect the biliary tract and promote the free flow of bile. Otherwise, medical treatment is purely palliative and analogous to that laid down for acute catarrhal jaundice.

### CHRONIC CATARRHAL CHOLANGITIS

**Etiology.**—Chronic catarrhal cholangitis may involve only the larger, especially the extrahepatic, ducts, or more or less of the entire biliary tract, or it may be confined to the finer intrahepatic ducts (radicular cholangitis or angiocholitis). Usually the lesions are widespread, involving the larger extrahepatic ducts, more or less of the larger intrahepatic ducts, and the gall-bladder. This form of the disease is due to the factors that provoke acute catarrhal cholangitis, and may result from repeated attacks of acute catarrhal cholangitis or from chronic low-grade infections. It is most commonly found in association with gall-stones,

with which its etiology and pathogenesis are so intimately associated that it will be discussed therewith; but chronic non-calculous cholangitis also occurs, being found in association with chronic gastroduodenal catarrh, after certain infections, in association with chronic obstruction, and in association with certain chronic disorders of the liver, such as hydatid cysts, chronic abscesses, etc. Chronic catarrhal radicular cholangitis or angiocholitis is rarely an independent affection.

**Pathology.**—The lesions consist of congestion and swelling of the mucosa, increased production of mucus, round-cell infiltration, and proliferation of the submucosa and muscularis, with the production of new fibrous connective tissue; these lead to thickening and induration of the walls of the ducts and to pericholangitis. There may be partial or complete obstruction of the ducts. In the event of complete obstruction, the ducts become enormously dilated (up to the size of a thumb or larger); the gall-bladder and some of the intrahepatic ducts also become dilated. The biliary tract usually contains a clear, almost colorless, often sterile mucus; when the mucus is sterile, the mucosa of the biliary tract is usually quite smooth. In the event of incomplete obstruction the ducts and especially the gall-bladder are less dilated, the contents are usually turbid and often contain bacteria, and the mucosa may be more or less ulcerated.

**Symptoms.**—The symptoms are those of chronic relapsing jaundice. Rarely this may represent a direct continuation of an acute catarrhal jaundice, being more insidious in onset, and subject to exacerbations and remissions. The attending phenomena are those of acute catarrhal cholangitis—prolonged. In the cases of complete obstruction, the contents of the biliary tract being sterile, there is usually no fever, and remissions in the jaundice are slight. In the cases of incomplete obstruction, remissions in the jaundice are more marked, and the contents of the biliary tract being infected, attacks of chill, fever, and sweats are common. These attacks by no means warrant a diagnosis of suppuration of the biliary tract, although they are evidences of infection. This chronic catarrhal cholangitis may lead to suppurative cholangitis (of which it is often only a minor manifestation), acute infectious jaundice, acute yellow atrophy of the liver, etc.

**Diagnosis.**—In cases of persisting jaundice that begin seemingly as acute catarrhal cholangitis, one must attempt to eliminate cholelithiasis and malignant disease obstructing the ducts. Often it is quite impossible to differentiate non-calculous from calculous cholangitis with a gall-stone in the common duct. A history of antecedent gall-stone colic is suggestive but by no means conclusive. Hypertrophic biliary cirrhosis may be eliminated by the absence of marked enlargement of the liver and spleen.

**Prognosis.**—This is dependent upon the associated lesions.

**Treatment.**—The treatment is essentially that of acute catarrhal cholangitis. In protracted cases operation should be undertaken with a view to drain the biliary ducts; this is the more demanded in view of the impossibility of excluding obstruction due to a gall-stone.



## ACUTE CHOLECYSTITIS

**Etiology.**—It is largely artifice that leads to a distinction between cholangitis and cholecystitis; the one like the other is an expression of infection of the biliary tract. In some cases the infection may remain confined to the ducts or the gall-bladder. In other cases, developing in the one or the other, the process may extend to that not primarily involved; and it may persist in the gall-bladder and subside in the ducts, or *vice versa*. A separate discussion of the two conditions seems warranted, however, because cholecystitis is characterized by certain definite features that develop largely because the gall-bladder is a closed sac with a small and readily obstructed exit, and because a common sequence of cholecystitis is cholelithiasis, which serves to keep active or readily induces cholecystitis.

Like cholangitis, cholecystitis results from bacterial infection, which is facilitated by any cause that reduces the resisting power of the gall-bladder or interferes with the free flow of bile. Mixed infections are not uncommon; and in some cases one organism having set up the lesions may die out spontaneously or be overgrown by another, whence in some cases the gall-bladder contents are sterile or the primary infectious agent eludes detection. The infectious agents reach the gall-bladder usually by way of the portal circulation or the general systemic circulation, although, of course, they may reach it by way of the diverticulum of Vater and the common bile duct. When cholecystitis or cholangitis complicates typhoid fever, pyococcic infections, etc., a natural inference is that the microorganismal cause of the general or primary infection is the cause of the local complication in the biliary tract—an inference usually but not always borne out by the fact. A biliary infection complicating or occurring sequentially to pneumonia, influenza, etc., may be due not to the specific cause of the general infection, but to pyogenic cocci or the colon bacillus, the original infectious agent or its toxin perhaps having prepared the way for the secondary invader. Certain zoöparasites also (especially round-worms, bilharzia) may invade the biliary tract, and reaching the gall-bladder may set up cholecystitis and subsequently cholelithiasis; in some cases, however, the zoöparasites act only as the carrier of other infectious agents.

**Typhoid Infections.**—Major importance and interest attaches to typhoid infections of the biliary tract.<sup>1</sup> It is now definitely known: (1) That the typhoid bacillus is regularly present in the gall-bladder, and commonly in pure culture, in practically all cases of typhoid fever; (2) that the typhoid bacillus may persist in the gall-bladder, as well as within gall-stones, years after the patient has recovered from an attack of typhoid fever; (3) that cholangitis and cholecystitis are by no means infrequent complications of typhoid fever; and (4) that a history of antecedent typhoid fever may be obtained in many patients with cholecystitis and cholelithiasis. The manifestations are various:

<sup>1</sup> Consult *Infections of the Biliary Tract*, by A. O. J. Kelly, *Am. Jour. Med. Sc.*, 1906, cxxii, 446, 744.

1. *Acute cholecystitis* occurring during the course of or after typhoid fever does not vary materially from acute cholecystitis due to other bacterial causes, although less likely to become suppurative.

2. The development of *gall-stones*.

3. *Primary typhoid cholecystitis*, often associated with cholangeitis; that is, an infection of the biliary tract with *Bacillus typhosus* without other evidence of past or present typhoid infection. The resemblance that many cases of infectious jaundice, Weil's disease, etc., bear to typhoid fever has been frequently commented upon, and it has, in fact, been suggested that Weil's disease is a modified form of typhoid fever. Possibly in many cases it is only typhoid (or paratyphoid) infection of the biliary tract.

4. *Chronic Carriers*.—In many cases the typhoid bacillus may be recovered from the gall-bladder years after an attack of typhoid fever.

Although bacterial infection is the essential factor in provoking acute cholecystitis, other factors are of contributing or predisposing importance; these are such as (1) reduce the vitality and resisting power of the gall-bladder and biliary ducts, and (2) interfere with the free flow of bile. Among the first mentioned are: trauma, such as blows and other injuries in the region of the gall-bladder, which rarely may reduce the resistance of the gall-bladder, and render it vulnerable to bacteria already present or that may be brought thither; a previous attack of cholecystitis and gall-stones, which favor infection; local diseases of the intestinal tract which may act as the source of the bacteria; and general disorders, such as Bright's disease, in which complicating or terminal infections are common. Among the conditions that act as predisposing causes by interfering with the free and unimpeded flow of bile are gall-stones, usually associated with chronic cholangeitis, tumors or foreign bodies (worms, etc.) within the ducts, tumors without the ducts, kinks or cicatrices compressing the ducts, etc.

**Pathology.**—Various types of acute cholecystitis may be differentiated—catarrhal, suppurative, phlegmonous, gangrenous, and membranous. Properly interpreted these are varying manifestations of the one process (an infection) which result from variations in the virulence of the infecting agent, in the local and general resistance and in the freedom of the circulation of the bile; they differ in degree rather than in nature, and pass sometimes almost imperceptibly the one into the others. In the mild grade of inflammation, so-called *acute catarrhal cholecystitis*, the gall-bladder is distended and tense; the wall is swollen, oedematous, and softened, and the mucosa is congested and covered with a layer of mucus. In many cases the inflammatory phenomena invade also the peritoneal covering, which then is covered with a thin layer of fibrin which may unite the gall-bladder to adjacent structures. The cystic duct usually is partially obstructed from swelling of the mucosa; sometimes it is completely obstructed, but usually only in the event of recurrent attacks of inflammation or of cicatrization of ulcerations. The contents of the gall-bladder usually consist of turbid bile; usually this is in excess and much thickened, inspissated, and tar-like; sometimes the contents consist of turbid, bile-stained, serous, or serofibrinous fluid;

rarely it may be stained with blood, in which event there is likely to be some erosion or superficial ulceration of the mucosa. Gall-stones may be encountered, especially in recurrent attacks; usually not in cases of less than four to six months' duration.

In the more severe, or *suppurative cholecystitis*, or acute empyema, the gall-bladder varies in size depending upon antecedent conditions. Should it have been previously normal or only slightly diseased and non-adherent, it may become considerably, sometimes very much, enlarged; but if previously the seat of cicatrization from chronic inflammation, no enlargement may occur; in this case it is usually united to adjacent tissues and organs by adhesions. The wall of the gall-bladder is softened, swollen, œdematous, congested, and usually very dark reddish, greenish, or blackish in color. The mucosa is congested and desquamated, and covered with a fibrinopurulent, sometimes also hemorrhagic, exudation. In many cases there is more or less ulceration, especially toward the fundus, in consequence of the relatively poorer vascular supply of the fundus and the gravitation of gall-stones. The ulceration may proceed through the wall and lead to perforation. The cystic duct is usually occluded even in the absence of gall-stones. The contents consist of turbid, bile-stained, fibrinopurulent, sometimes sanguinolent fluid; gall-stones are present in about 80 per cent.

In some cases the phenomena are less acute; the congestion and softening of the wall are less marked or entirely absent, the wall then being thickened and indurated; there is little if any pericholecystitic fibrinous exudation, although the gall-bladder may be firmly united to adjacent organs; the mucosa of the gall-bladder is more or less ulcerated and the contents are more or less purulent—cases of so-called *chronic empyema of the gall-bladder* or *chronic ulcerative cholecystitis*. On the other hand rarely the lesions may be more acute than in the more common cases of acute suppurative cholecystitis; the œdematous, hemorrhagic, and purulent infiltration of the gall-bladder is widespread, and may lead to extensive dissection of the different coats, the separation, for instance, of the mucosa from the underlying coats, or extensive sloughing with or without perforation—so-called *phlegmonous cholecystitis*. A further or more advanced and rare stage is spoken of as *gangrenous cholecystitis*, a term very inconsiderately employed. The small foci of necrosis that occur in suppurative cholecystitis, for instance, are sometimes spoken of as localized gangrene—ulcerative cholecystitis being a more preferable term. When, however, a large section of the gall-bladder becomes necrotic the term gangrenous cholecystitis is not inaptly applied. This results from very virulent infection, or interference with the blood-supply due to a gall-stone impacted in the neck of the gall-bladder or in the cystic duct, or to infectious thrombosis of the nutrient artery. The lesions resemble those of advanced suppurative or phlegmonous cholecystitis, with the addition of complete necrosis or gangrene of a variable portion of the gall-bladder; the gangrene usually begins at or near the fundus (where the blood-supply is poorest) and spreads toward the neck; in some cases it begins about a gall-stone more or less firmly embedded in the wall of the gall-bladder. *Membranous*,



*cholecystitis* is a rare condition characterized by the formation of a membranous or fibrinous coat of the interior of the gall-bladder, and perhaps of the biliary ducts. It is usually associated with gall-stones, and with mucous enteritis or colitis.

**Symptoms.**—Acute cholecystitis is extremely variable in its symptomatology. In many cases it is altogether latent; in other cases, although it occasions obvious symptoms, the true nature of these is often masked, and they escape correct interpretation, being commonly regarded as evidences of disordered stomach. Thus, for instance, during typhoid fever, but also in other circumstances, there are: (1) Cases in which a noteworthy enlargement of the gall-bladder occurs; but the biliary ducts being patent, the drainage sufficient, and the patient's sensibilities somewhat obtunded, there is no complaint and the disorder escapes recognition, unless systematic examinations of the gall-bladder region are undertaken; in this event a more or less enlarged and tender gall-bladder may be encountered. It is surprising how frequently this condition occurs and how frequently it goes undetected. (2) There are cases in which a little epigastric discomfort, perhaps slight nausea, in some cases actual pain, is complained of, and examination reveals an enlarged and tender gall-bladder. (3) Cases in which, announced by the ordinary symptoms, acute cholecystitis or cholangitis develops.

Initial nausea and vomiting, fever, pain, and tenderness in the region of the gall-bladder, rigidity of the overlying abdominal muscles, and an enlarged and tender gall-bladder constitute the important clinical manifestations of acute cholecystitis. These may be of sudden or rather insidious onset. The nausea and vomiting are usually moderate and soon subside, except in the event of pericholecystitic or more general peritonitis and concomitant paresis of the intestine. In catarrhal cholecystitis the fever is slight and lasts only a short time; in the cases complicating some general infection there may be little if any added fever, but if occurring, for instance, during convalescence from typhoid fever, the onset of the cholecystitis is usually announced by fever, which may be high. The *pain* usually occurs first in the epigastrium, sometimes directly in the midline, and later becomes more localized to the right hypochondrium; it varies much in character. In some cases it is dull and aching; in other cases it is sharper and more severe, and while continuous is subject to acute exacerbations; in perhaps the majority it is severe and paroxysmal and resembles or is identical with the pain of so-called gall-stone colic. The complaint of pain is much influenced by the mental state of the patient: in acute infections attended by mental torpor due to toxemia there may be little or no complaint of pain, but there may be considerable local tenderness. The pain may be referred to the region of the right scapula, as in gall-stone colic, or to the right shoulder when the peritoneum is involved, or downward to the right lower abdominal quadrant, and suggest appendicitis; as a matter of fact, the two conditions cholecystitis and appendicitis may be concurrent.

There is more or less tenderness in the right upper abdominal quadrant. At first this may be diffuse, but usually it soon becomes localized to the

region of the gall-bladder. The overlying muscles are rigid, and in consequence sometimes simulate a tumor of the gall-bladder. In most cases, however, by careful palpation one can feel an enlarged and tender gall-bladder; in many cases it is also visible. The degree of enlargement varies considerably in recent cases in which the gall-bladder is non-adherent and there is little pericholecystic exudation. The tumor, corresponding with the enlargement of the gall-bladder, is pear-shaped, tense or semifluctuating, moves with respiration, and is displaceable by palpation, although both of these may be inhibited by the attendant pain; in older or recurrent cases, in cases in which there are old adhesions, and in cases in which there is considerable pericholecystitic serofibrinous and other exudation, and perhaps also involvement of adjacent tissues (with intestinal paralysis, tympanites, abscess formation, etc.), the tumor mass is likely to be more globular or irregular, or ill-defined, and it may not move at all on respiration or be displaceable on palpation. Usually the mass is in the region of the gall-bladder, and as it increases in size it advances toward the umbilicus; but in a considerable number of cases it descends in the flank; sometimes it is found so low as to suggest periappendicular suppuration. With the progress of the disease the tumor often can be observed gradually to increase in size. As the inflammatory phenomena subside and the cystic duct again becomes patulous, the tumor decreases in size and may ultimately disappear. Some local tenderness especially on deep palpation, however, usually remains for some days or weeks. Bahr<sup>1</sup> has called attention to certain cases masquerading as bronchitis, in which the only symptoms point to the lungs and bronchi. Slight dulness with râles accompanied by fever and later slight jaundice characterize the attacks which may be numerous.

Jaundice is not a part of uncomplicated cholecystitis; its development signifies extension of the inflammation of the ducts (cholangitis), spasm of ducts, or some complication such as gall-stones obstructing or compressing the hepatic or the common duct. The liver is not enlarged unless there is cholangitis. The pulse may be normal or slightly accelerated. Usually there is a moderate leukocytosis (12,000 to 15,000).

The *consequences* of acute cholecystitis are many and various, and of much clinical importance. In the majority of cases, especially in those occurring during general infections, such as typhoid fever, the clinical manifestations subside at the end of four or five to ten or fourteen days; perhaps in some of these cases the lesions also subside and the gall-bladder returns to its previously normal condition. In the great majority of cases the lesions become chronic, the infection becomes latent for a time and of minor grade: the usual consequence of this is gall-stone formation; but chronic cholecystitis may ensue without gall-stone formation. In many cases after the formation of the gall-stones the infection gradually dies out, and the gall-stones may remain latent, perhaps throughout life, although the gall-bladder in such circumstances is disposed to ready reinfection. Sometimes, especially if the infection was slight in grade and soon died out, and if a gall-stone obstructed the

<sup>1</sup> *Münch. med. Wchenschr.*, 1912, lix, 2326.

cystic duct or the exit of the inflammatory exudation was otherwise prevented, the contents of the gall-bladder soon take on a serous or mucous character, and a condition of cystic distension or hydrops of the gall-bladder results. In other cases the gall-bladder remains continuously infected; in other cases the patient may suffer from minor phenomena due to chronic cholecystitis (with or without gall-stones), and in addition become subject to repeated recurring attacks of acute cholecystitis (reinfections or exacerbations of a chronic infection); in either case the lesions are likely to become suppurative or ulcerative—so-called chronic *empyema* of the gall-bladder. Again, although the lesions of the gall-bladder subside, adhesions have developed between the gall-bladder and adjacent organs, which often engender serious consequences. In some cases of acute cholecystitis the lesions do not subside; they progress to the more serious forms of the disease—suppurative, phlegmonous, or gangrenous cholecystitis; but suppurative phlegmonous and gangrenous cholecystitis may also develop suddenly, as a primary manifestation of an infection; in about 80 per cent. of the cases, however, they occur in connection with gall-stones, therefore in chronic infections or reinfections. The clinical manifestations consist of an aggravation of the symptoms of acute cholecystitis. The evidences of local inflammation, peritonitis, are more severe; in some cases persistent nausea, vomiting, widespread abdominal pain and tenderness, tympanites, constipation, etc., suggest infection of the general peritoneal cavity. Occasionally the manifestations are those of acute rapidly developing general peritonitis without localizing symptoms. The gall-bladder, as a rule, is palpable—near the tip of the ninth costal cartilage in case it is incapable of little if any distension, or near the umbilicus, in the flank, or in the right inguinal region in case it has become much distended. In many cases it is quite low, being associated with cholelithiasis and linguiform lobulation (Riedel's lobe), and may simulate appendicitis. Jaundice is not a necessary symptom, but it occurs more frequently in the severer than in the milder form of acute cholecystitis, because of the associated lesions, such as gall-stones and tumors obstructing the ducts, and the more common occurrence of cholangitis. The temperature is usually high ( $103^{\circ}$  to  $104^{\circ}$ ), and commonly accompanied by chills and sweats; but in some cases of severe infection, with minor resistance on the part of the patient, the temperature may be lower. The pulse is accelerated, 120 or more—which is a better indication of the seriousness of the patient's condition than the temperature. Usually there is a polynuclear leukocytosis of from 15,000 to 35,000 or more.

Perforation of the gall-bladder may occur: into preformed adhesions, and lead to the development of a localized abscess, which, if the adhesions involve the abdominal wall, may become manifest by local œdema and other signs of inflammation; into the liver, and lead to a liver abscess; into the general peritoneum, and lead to widespread purulent peritonitis; into the hollow abdominal viscera, and lead to fistulæ, etc. Sometimes the onset of the perforation is announced by sudden increase of the local pain, more or less collapse, increased pulse rate, and progression of the local abdominal and the general symptoms; but, as in appendicitis, the



symptoms often only steadily increase, and no time can be set as that of the occurrence of perforation.

**Diagnosis.**—The diagnosis of acute cholecystitis presents no serious difficulties in the great majority of cases: nausea and vomiting, pain and tenderness in the region of the gall-bladder, rigidity of the overlying abdominal muscles, and an enlarged and tender gall-bladder constitute a complex of symptoms that can scarcely be attributed to anything else. In some cases the symptoms are not obtrusive, and the enlarged and tender gall-bladder must be sought, but even these cases present no diagnostic difficulties. The phenomena of gall-stone colic also are properly attributable to an acute (perhaps acute exacerbation of a chronic) cholecystitis, and the local pain and tenderness and rigidity of the overlying muscles, if sought, will usually be found. The more serious forms of cholecystitis are to be distinguished from the milder or catarrhal form, usually by their more abrupt onset, or abrupt increase in severity, and by the more marked local and general symptoms, that is, more evident and perhaps widespread peritonitis and more serious toxemia, and by the fact that in most cases there is a history of antecedent cholecystitis or cholelithiasis. The onset of perforation or gangrene can rarely be diagnosed with certainty, except perhaps by a sudden increase in abdominal pain, with collapse, increased pulse rate, and spreading peritonitis; it should be suspected in the event of sudden fulminating peritonitis occurring in a chronic cholecystitic or cholelithitic subject, especially if the lesions began in or remain limited to the upper abdomen. In this event one must exclude other causes of peritonitis, in which a study of the patient's past history is of the utmost importance.

Difficulty may be experienced in differentiating acute *appendicitis*, particularly in those cases in which the enlarged gall-bladder is unusually low and perhaps projects into or is situated in the right iliac fossa; but cholecystitis is suggested by previous attacks of so-called dyspepsia or of more obtrusive symptoms of cholelithiasis or cholecystitis, especially if associated with jaundice, by relationship of the attacks to dietetic indiscretions, by limitation of the pain to the epigastrium or the right hypochondrium and radiation to the right shoulder (the pain is rarely as diffuse as is often the case in early appendicitis), by the presence of a zone of cutaneous hyperalgesia (Head) about the upper right half of the abdomen, by the fact that the mass (enlarged gall-bladder) often moves with the liver during the phases of respiration, etc.

**Prognosis.**—In the majority of cases the prognosis in acute cholecystitis is good, the process tending to subside, under appropriate treatment, within ten days or a fortnight; the mildest cases may subside within four or five days or a week; the inflammatory and retained secretions are discharged through the cystic duct and the gall-bladder reverts to its normal size. Sequels, especially gall-stones and adhesions, however, are almost certain to occur, so that the subsequent outlook is not the best; in other cases a low-grade infection may persist and the patient become a subject of chronic infection and recurring attacks of cholecystitis. In the more severe forms, suppurative, phlegmonous, and gangrenous cholecystitis, the tendency toward spontaneous cure is slight.

In this event the prognosis is grave, since not only are the lesions serious in themselves but a localized excess or general peritonitis may ensue and a fatal issue result, unless recourse is had to surgical intervention. Occasionally in these serious cases the obstruction of the cystic duct may be due only to swelling of the mucosa; in this event it may lessen, and part, at least, of the contents of the gall-bladder may be discharged; but if the acute inflammatory lesions subside, chronic empyema is likely to ensue. In some cases the infection is so virulent that extensive phlegmonous inflammation or gangrene develops before limiting adhesions can form. The prognosis in these cases is extremely grave, death usually resulting unless the patient is operated upon.

**Treatment.**—This in general is that recommended for gall-stone colic, which virtually is an attack of more or less acute cholecystitis. The diet should be reduced to a minimum; perhaps withheld altogether for a day or two, if the patient's general condition permits. Until the acute phenomena subside the diet should be bland and easily digested: milk and Vichy or lime-water, broth, cereals, etc. The bowels should be opened by enemas of hot water for the first day or two, whereupon Carlsbad salts or sodium phosphate or similar salts in hot water should be given. It is wise to withhold morphine, which, unless required to mitigate acute suffering, tends to mask symptoms, to promote a false security, and is otherwise objectionable. Relief from pain usually follows hot fomentations to the region of the bladder, lavage of the stomach with hot alkaline water, a full hot bath, etc.; if not, a small dose of morphine ( $\frac{1}{16}$  to  $\frac{1}{32}$  grain) may be tried; a very small dose is often extremely efficacious. Nausea and vomiting depend upon the same factors as the pain, and they usually subside with the pain. Following subsidence of the acute phenomena the treatment recommended for cholelithiasis should be instituted.

Happily most cases of acute cholecystitis gradually subside; occasionally the local symptoms increase, evidences of more or less extensive peritoneal irritation or actual peritonitis supervene, the temperature, leukocytosis, and other manifestations of infection increase; the local lesions have progressed to suppuration, necrosis, or gangrene. In this event the necessity of operative intervention must be considered.

### CHRONIC CHOLECYSTITIS

**Etiology.**—Chronic cholecystitis may be the residual manifestation of an acute cholecystitis, or the process may be chronic from the beginning. Its etiology is that of acute cholecystitis, the chronicity of the process being a manifestation of lingering infection, or the consequence of very low-grade infection with almost but not quite sufficient biliary drainage. In the great majority of cases the condition is associated with gall-stones, the one process sustaining the other; that is, most cases are calculous cholecystitis; in a few cases the lesions extend throughout the biliary tract; that is, cholangitis and cholecystitis are associated.

**Pathology.**—The process may or may not be associated with gall-stones. In absence of gall-stones the lesions may be catarrhal, that is virtually

confined to the mucosa, which shows more or less congestion, swelling, desquamation, and increased formation of mucus; the gall-bladder usually is distended and filled with thick tenacious bile or bile and mucus. In some cases the mucosa is thinned and atrophic, especially in spots, evidently the consequence of past erosion or ulceration. In many cases of long standing the gall-bladder becomes reduced in size, very small, and sclerotic; it may be represented by a mass of thickened contracted connective tissue, perhaps tightly enclosing one or more gall-stones, but sometimes not. When thus small and shrivelled, the gall-bladder, whether containing gall-stones or not, often makes up part of a mass of firm adhesions that bind together the adjacent tissues; in many cases the gall-bladder can scarcely be identified as such. The cystic duct is often, perhaps usually, patulous, but it may be partially or completely obstructed. In some cases the tissue adjacent to the gallstones, or, in their absence, that lining the still-persisting lumen, is made up largely of cicatrizing granulation tissue, and may reveal no vestige of mucosa; in other cases the lining epithelium has invaded the deeper layers of the walls and is clearly hyperplastic and irregularly proliferated (beginning carcinoma). The musculature is usually atrophic, and replaced by fibrous connective tissue.

**Symptoms.**—These are of cholelithiasis—which is the important concomitant of chronic cholecystitis. A clinical differentiation between cholecystitis with and without cholelithiasis may be attempted, but those with most experience find it increasingly difficult to determine whether or not gall-stones are present in individual cases.

**Diagnosis.**—It is practically impossible in most cases to say definitely whether or not gall-stones are present. The likelihood of their being present is enhanced by repeated attacks of severe colic followed by jaundice, but colicky pains are present in many cases (70.6 per cent.) without gall-stones, and jaundice may occur in 35.3 per cent. of cases without gall-stones. The detection of faceted gall-stones in the stools suggests the presence of others in the gall-bladder. The absence of gall-stones in a case of chronic cholecystitis can scarcely be postulated with the knowledge at hand.

The *prognosis* and *treatment* are the same as in cholelithiasis.

### CHOLELITHIASIS<sup>1</sup>

**Etiology.**—Cholelithiasis is an exceedingly common condition, being found at autopsy in from 5 to 10 per cent. of subjects dead from all

<sup>1</sup> The literature of cholelithiasis is extensive. The more important monographs comprise: Naunyn, *A Treatise on Cholelithiasis*, 1896; Kehr, *Gall-stone Disease*, 1901; Mayo Robson, *Diseases of the Gall-bladder and Bile Ducts*, third edition, 1904; Moynihan, *Gall-stones and their Surgical Treatment*, second edition, 1905; Bland-Sutton, *Gall-stones and Diseases of the Bile Ducts*, 1907; Aschoff and Bacmeister, *Cholelithiasis*, 1909. Virtual monographs are contained also in Nothnagel's *Encyclopedia of Practical Medicine*, article by Hoppe-Seyler, and in Rolleston's *Diseases of the Liver, Gall-bladder, and Bile Ducts* (literature). Valuable articles by Ewald, Musser, Brewer, Herter, Mayo, and Kehr are contained in the *Tr. Cong. Am. Phys. and Surg.*, 1903, vi. The results of considerable personal experience will be found in the following articles: Deaver, *Am. Jour. Med. Sc.*, 1908, cxxxv, 137, cxxxvi, 625; Mayo, *Ann. Surg.*, 1906, xlv, 209; Richardson, *Boston Med. and Surg. Jour.*, 1906, clv, 329; 1907, clvi, 687; and Kehr, *2me Cong. de la Soc. internat. de Chir.*, Brussels, September 21-25, 1908. Moynihan, *Brit. Med. Jour.*, 1908, ii, 1598; 1913, i, 8.



causes. It is specially prevalent in the temperate zones, being quite uncommon in the tropics. It occurs at all ages, but the incidence increases progressively with advancing years: 75 per cent. or more of the cases are found in persons over forty years of age, and less than 1 per cent. in those under twenty years; but this age incidence does not correctly represent the time of the formation of gall-stones, since in many cases, having formed, they remain latent for years and are found only when the subject dies at a more advanced age. Doubtless many if not most gall-stones are formed in early adult life, before the fortieth year, corresponding with the period of greatest frequency of typhoid and other infections, etc. Rarely the disorder is encountered in infancy or childhood. The majority of cases in infancy are doubtless due to intra-uterine infection, the process perhaps being analogous to that which in other circumstances induces congenital obliteration of the bile ducts; the cases found in older children also may have originated during fetal life and remained latent for a number of years, but it is not always possible to exclude postnatal typhoid and other infections. Gall-stones are more common in women than in men, the ratio being variously stated as 5 to 1 (Schroeder) to 4 to 3 (Rolleston).

The one necessary factor is a low-grade catarrhal inflammation of the biliary tract; the second requisite seems to be some obstruction to the free flow of bile. The one without the other factor is not sufficient; whether a third factor is of significance remains to be determined. The catarrhal inflammation of the biliary tract is set up especially by typhoid and colon bacilli; but also apparently by attenuated streptococci, staphylococci, and other microorganisms that may cause acute cholecystitis; perhaps also by anaërobic bacteria. It is essential that the antecedent catarrh be mild in grade, since in severe infections the mucosa of the gall-bladder is likely to be more or less destroyed and its cholesterol-producing function abolished. The infective agents usually reach the gall-bladder by the portal circulation; variations in the source and pathways of infection are similar to those mentioned in connection with acute cholecystitis. Kuru<sup>1</sup> has studied by means of Weigert's fibrin stain sections of gall-stones and calls attention to the importance of fibrin in their production.

Apart from infection of the biliary tract, a secondary requisite seems to be some obstruction to the free flow of bile. This occurs in circumstances similar to those mentioned in connection with acute cholecystitis; but there are also a number of additional contributing factors. Thus gall-stones are especially common in those who lead a sedentary life as contrasted with laborers and others who work much outdoors, in women as contrasted with men, etc.; as part of the general muscular inactivity, the abdominal muscles and the diaphragm, contract relatively feebly and the bile, inefficiently expelled, stagnates in the gall-bladder.

In women a number of factors contribute. In addition to a more sedentary life, they are more often the subject of hepatoptosis or nephroptosis, that occasion more or less marked and continuous distension of

<sup>1</sup> *Arch. f. path. Anat.* (etc.), Berl., 1912, cex, 433.

the abdomen and interfere with the movements of the diaphragm. In consequence of the prolapse of the liver, the gall-bladder becomes dependent and the cystic or the common bile duct kinked, or perhaps has considerable traction brought to bear upon it and becomes obstructed, so that the gall-bladder is less easily emptied than in health and is more disposed to infection. Tight lacing may act in a similar manner. The frequency of pelvic infections may be of some etiological significance, either by serving as the source of the infection or leading to the formation of adhesions. The association of cholelithiasis with pregnancy is undeniable, but its importance is difficult to estimate, since the great majority of middle-aged women, whether or not they suffer from gall-stones, have been pregnant; there is some evidence, however, that gall-stones are more common in those who have been pregnant, especially repeatedly pregnant, than in those who were never pregnant. Perhaps in some cases puerperal infections are the cause of the gall-stones; sometimes the biliary infection, although often misinterpreted, can be definitely determined to have been acquired during the puerperium. Cholelithiasis is sometimes found with appendicitis; when the appendicitis precedes, the cholelithiasis and cholecystitis may have resulted from the transport of infection by the portal circulation; when the cholecystitis precedes, the appendicitis may perhaps result from the lodgement of infection in an unusually vulnerable organ.

Gall-stones show a relatively increased incidence in certain forms of heart disease, especially mitral and aortic valvular disease. This is doubtless due to several factors: the more sedentary mode of life incumbent upon chronic cardiac subjects, and the chronic congestive processes obstruct the flow and perhaps cause inspissation of the bile, reduce the resistance of the biliary tract, and favor infection. Similar factors account for the relative increase in the incidence of gall-stones in certain chronic pulmonary diseases.

Diet, disorders of the gastro-intestinal tract, and disorders of metabolism have long been credited with more or less etiological significance, but their exact influence is difficult to determine. Disorders of the gastro-intestinal tract associated with catarrh doubtless are of significance, since they may lead to extension of congestive processes to the biliary tract, provide bacteria that may induce catarrhal disorders in the bile ducts, and are a fruitful source of many toxic products that exert a deleterious influence on the biliary passages. Dietetic and other indiscretions that lead to gastro-intestinal catarrh are of at least indirect influence in causing gall-stones; and a vicious circle is formed in that cholelithiasis and the antecedent cholecystitis not only are frequently manifested by misinterpreted symptoms of so-called dyspepsia or indigestion, but lead directly to gastro-intestinal catarrh, and in virtue of the commonly associated precholecystic adhesions induce much more serious disturbances of the stomach and intestines. Constipation, an expression of or associated with dietetic indiscretions, sedentary habits, etc., is probably of some etiological significance in itself, largely on account of the attendant sluggishness of the intestinal circulation.

Whether diet as such is of real etiological significance is difficult to

determine. Heavy eating and the excessive use of alcohol are doubtless of importance, especially by virtue of the gastro-intestinal catarrh and the chronic congestion of the portal system that they lead to; whether they are of additional significance, by virtue of disturbances of metabolism, is not definitely known, although it is widely and has long been believed in. Perhaps an excessive amount of food is of more significance than its character, although it is said that a carbohydrate or fatty diet disposes to, and a protein diet disposes against, the formation of gall-stones. The matter is largely speculation. Since it has been definitely determined that the precipitation of cholesterin is due to catarrh of the biliary tract, the supposition that a carbohydrate diet leads to such precipitation by reducing the bile acids, the solvents of cholesterin, has lost much of its supposed importance, and this has been totally destroyed by Naunyn's statement that even in diseased conditions the bile scarcely if ever contains so much cholesterin that it cannot take more in solution. Miyake<sup>1</sup> found gall-stones in but 3.05 per cent. of 8406 autopsies in Japan. The sexes were nearly equally affected. Japanese women do not wear corsets and Miyake believes this reduces the incidence in the female sex.

**Pathology.**—Gall-stones may be single or multiple; there may be one or thousands (7802 in a case of Otto's). In most cases the number varies between a dozen and a hundred; most of those in excess of a hundred are small and inconsequential, and are spoken of as biliary sand or gravel. The stones vary much in size—from the smallest particle to those larger than a normal gall-bladder. Merkel found a gall-stone measuring 15 cm. in length and 12 cm. in circumference; and Frerichs reports one that weighed 120 grams, and Ritter one that weighed 135 grams. When there are many stones, most of them are usually small; when there are few, there may be several rather large stones; when there is only one, it may be small, moderate in size, or very large, even completely filling a distended gall-bladder. Gall-stones vary also in shape. The large single stones, or several stones that fit together (obviously resulting from fracture of a single large stone), conform to the shape of the interior of the gall-bladder, and are therefore ovoid or somewhat pear-shaped. Small single stones are usually ovoid or spheroidal. Multiple stones are usually cuboid or polyhedral, and exhibit variously shaped surfaces (facets), triangular, quadrangular, polygonal, etc., which being opposed to one another are usually smooth and polished, although it is doubtful if this results, as is supposed, in consequence of mutual attrition; the edges of these stones are rounded rather than sharp. Stones within the intrahepatic ducts conform to the ducts in shape, and are ovoid or cylindrical; occasionally they are branched, as are the ducts. Although usually smooth, the surface of gall-stones may be rough, irregular, or nodular (mulberry calculus). In consistency gall-stones vary, depending upon the age and the chemical composition, the recently formed and the cholesterin stones being the softest; older stones may be hard and crumble readily, especially after being dried.

<sup>1</sup> *Archiv f. klin. Chir.*, 1913, ci, 54.



The following varieties of gall-stones are distinguished by Naunyn: (1) Pure cholesterin stones, which consist of nearly pure cholesterin and are uncommon. They vary in size from that of a cherry to that of a pigeon's egg, are hard, oval, or roughly spherical, seldom faceted, have a smooth or nodular surface, and are pure white or yellowish and translucent, or rarely brown, greenish, or brownish black on the surface. On section they are white and crystalline throughout, or show brown deposits between the crystals; they are not stratified. (2) Laminated cholesterin stones, which consist of about 90 per cent. of cholesterin, together with bilirubin calcium, biliverdin calcium, and calcium carbonate. In general appearance they resemble the pure cholesterin calculi, but they may be brittle and friable, and they are often faceted. On section they are more or less distinctly laminated, layers of almost pure white alternating with others that are yellow, brown, green, or red. The centre may be crystalline, but the external layers are usually vitreous or earthy. (3) The common (or mixed cholesterin) stones, which vary much in size, although they seldom equal a large cherry; they may be small and very numerous, and are usually faceted. The surface is usually yellow, but often brown or white. When fresh they are often soft and greasy; when dried they undergo shrinkage and become harder. On section the centre is often soft and may contain a cavity. (4) Mixed bilirubin-calcium stones, which may consist roughly of 75 per cent. of bilirubin calcium, and about 25 per cent. of cholesterin. They are as large as a cherry or larger, and may occur singly or in groups of three or four in the gall-bladder or larger ducts. Their shape depends upon their situation; when multiple they may be faceted. They consist of concentric layers of reddish-brown or dark-brown material, which is seldom quite hard, and contracts on drying often with the formation of fissures or cracks. (5) Pure bilirubin-calcium stones, which vary in size from that of a grain of sand to that of a pea. There are two types: small, solid, brownish-black concretions, with rough irregular surfaces and wax-like consistency, and exhibiting a disposition to become welded; and harder, smooth concretions of a grayish-black metallic lustre and an internal spongy structure. (6) Rarer stones, such as amorphous and incompletely crystalline cholesterin gravel (resembling pearls); calcareous stones; concretions with included bodies and conglomerate stones; and casts of the bile ducts.

Gall-stones may be found in any part of the biliary tract. Of 216 patients operated upon for infections of the biliary tract by John B. Deaver at the German Hospital, Philadelphia, 182 (84.2 per cent.) had gall-stones and 34 (15.8 per cent.) had no gall-stones. Of the 182 that had gall-stones, 101 (55.5 per cent.) had stones in the gall-bladder alone; 23 (12.5 per cent.) had stones in the gall-bladder and cystic duct; 19 (10.5 per cent.) had stones in the gall-bladder and common duct; 12 (6.6 per cent.) had stones in the common duct alone; 11 (6 per cent.) had stones in the cystic duct alone; 5 (2.8 per cent.) had stones in the gall-bladder, cystic, hepatic, and common ducts; 4 (2.2 per cent.) had stones in the gall-bladder, cystic, and common ducts; 2 (1.1 per cent.) had stones in the adhesions (not otherwise specified); and 4 (2.2 per cent.)

had stones in regions not definitely specified. Of the 216 patients, 58 had no stones in the gall-bladder, and of these, 23 had stones in the ducts; 41 had stones in the common duct, and of these, 12 had stones nowhere else; 9 had stones in the hepatic ducts (as well as elsewhere).

**Pathogenesis.**—In consequence of bacterial infection of the biliary tract a low-grade catarrhal inflammation is set up; this, on the one hand leads to obstruction to the free flow of bile from swelling of the mucous membrane, and the products of this inflammation contain the essential constituents of gall-stones. In the gall-bladder the catarrhal inflammation leads to desquamation of the lining epithelium, an albuminous exudation, and an increased formation of mucus and of cholesterin; and in the gall-bladder dynamic factors frequently favor the stagnation of bile. The increased cholesterin is not derived from the bile; it results from catarrhal disintegration of the mucous cells lining the wall of the gall-bladder. The second important constituent of the gall-stones, bilirubin-calcium, is derived from the bile, being precipitated by bacterial growth or by the albuminous exudation of the inflammatory process—a phenomenon that can be imitated experimentally by adding egg-albumen to normal bile. Bacmeister<sup>1</sup> and Exner and Heyrovsky<sup>2</sup> have shown that bacteria, notably the typhoid and the colon bacillus (but not streptococci), may effect directly a decomposition of the bile with the precipitation of cholesterin. Exner and Heyrovsky attribute this to decomposition of the bile-acid salts (the solvent menstruum), in consequence of which the normal amount of cholesterin is no longer held in solution. Stagnation and inspissation of the bile do not give rise to the increased formation of cholesterin nor to the precipitation of bilirubin-calcium—whence they are contributing factors only. Bilirubin-calcium is believed by Naunyn to act as a cement substance, binding together the cholesterin, desquamated epithelium, etc., the whole forming the nucleus of the gall-stone. The exact significance of foreign bodies and of chemical substances apart from bacterial products has not yet been definitely determined. There being no cholesterin-bearing mucous membrane in the smaller bile ducts, cholesterin gall-stones are not formed within the intrahepatic ducts, although by a retrograde movement they may be transported thither; bilirubin-calcium stones only are formed in the intrahepatic ducts; but both varieties are formed within the gall-bladder.

**Associated Lesions.**—The lesions of cholecystitis and cholangitis are common concomitants—so-called calculous cholecystitis and cholangitis. The gall-stones may be free in the gall-bladder or the ducts, although usually more or less confined by the associated chronic inflammatory processes; in some cases the stones may be quite adherent to the mucosa, especially in the gall-bladder; in other cases there is more or less incrustation of the wall, a deposition in the wall of cholesterin.

The consequences of gall-stone activity may be mechanical or inflammatory or both. The mechanical consequences follow what may be designated wandering of the stone into and through the biliary passages. Probably the most important and serious effects comprise permanent and

<sup>1</sup> *München. med. Wchnschr.*, 1908, lv, 211, 283, 339.

<sup>2</sup> *Wien. klin. Wchnschr.*, 1908, xxi, 214.

complete obstruction of the common bile duct. Of only less importance are the dragging sensations and discomfort attendant upon the weight of many gall-stones in a distended gall-bladder; the gradual production of a Riedel or a linguiform lobe of the liver; the effects of pressure on adjacent organs; complete obstruction of the cystic duct, which, as a rule, leads at first to some distension of the gall-bladder, but soon to absorption of the bile and its replacement by mucus (hydrops) and gradual shrinkage of the gall-bladder, etc. These acquire their major importance from the opportunity that they afford for bacterial infection.

This *infection* of the biliary tract is of the utmost significance, and forms an integral part of so-called calculous cholecystitis and cholangitis. The ensuing lesions are of the greatest diversity. The concomitant inflammatory phenomena may be of varying grades—from the mildest catarrhal lesions to widespread phlegmonous and ulcerative processes; gall-stones, if present, may be quiescent or active; they may cause an acute or chronic, partial or complete, temporary or permanent, obstruction of the cystic, the hepatic, or the common bile ducts, and, on the other hand, such obstruction may occur in the absence of gall-stones (being due to swelling of the mucous membrane, kinking of the ducts, or obstruction from without), and in the presence of gall-stones the ducts may be partially or completely patulous; the gall-bladder may be distended or contracted, its walls thinned or much thickened, and its lumen ultimately may become almost if not quite obliterated; it may contain bile, mucus, blood, or pus, or combinations of these, in addition to or in the absence of gall-stones; adhesions may form between the gall-bladder and adjacent structures, and by way of the adhesions the gallstones may rupture into the gastro-intestinal tract and sometimes cause intestinal obstruction; or purulent pericholecystitis and pericholangitis, localized or generalized peritonitis, pyelephlebitis, pericholangitic abscesses of the liver, fistulæ, acute and chronic pancreatitis, etc., may ensue; and finally, in some cases, a general bacterial, often pyococcic infection, with or without multiple abscesses, may develop.

**Symptoms.**—The symptomatology of gall-stones is extremely variable, and one may perhaps speak of the immediate and the remote consequences, but in many cases differentiation is quite impossible. One may also speak of the mechanical and the infectious phenomena, the aseptic and the septic phenomena of the French writers; this in many respects is a serviceable classification, but the one set of phenomena by no means can always be differentiated from the other, and the one frequently follows the other or they occur together. The symptomatology is further complicated by the fact that in different cases the symptoms may be due to the gall-stones themselves, or to the associated infectious cholecystitis or cholangitis, pericholecystic adhesions, disease of related or adjacent organs, etc. One may, however, differentiate (1) a general symptomatology, and (2) certain special phenomena due to obstruction of the cystic duct, or (3) of the common duct, and (4) certain complications and sequels.

**General Symptomatology.**—The characteristic and significant symptoms are; (1) Chronic, long-continued, or recurring indigestion, called by



Moynihan "inaugural symptoms," and (2) the phenomena designated gall-stone colic. The symptoms of chronic long-continued or recurring indigestion are of the utmost importance and are commonly misinterpreted. This stands in relationship with the facts—that gall-stones are present in very many subjects and are commonly believed not to cause noteworthy symptoms; that symptoms, having once occurred, are exceedingly likely to recur; and that the symptoms are often paroxysmal and very severe.

It is often said and widely believed that gall-stones are usually latent, and that only a very small percentage of gall-stone subjects (commonly estimated at 5 per cent.) manifest noteworthy symptoms thereof. Gall-stones are sometimes latent, particularly in elderly subjects in whom the original infection has died out, and in whom more or less atrophy, especially of the muscular coat of the gall-bladder and biliary ducts, has occurred; but it is now well known to surgeons, although less widely acknowledged by general practitioners, that the symptoms commonly denominated "stomach trouble," "indigestion," "dyspepsia," etc., are due in many cases to disease of and about the biliary tract. In a number of cases in which gallstones are an accidental finding at the necropsy, investigation of the past history reveals many and often long-continued attacks of "indigestion;" the stomach is often found normal—in which event the gall-stones, cholecystitis, or precholecystic adhesions, rather than being accidental, serve to explain the clinical symptoms. Moynihan<sup>1</sup> thus describes his so-called "inaugural symptoms." "The patient complains of a fullness, weight and distension or oppression in the epigastrium coming on soon after meals, within half or three-quarters of an hour, relieved by belching and dismissed almost on the instant by vomiting, elicited with remarkable constancy by certain articles of diet, especially those of a 'greasy' nature and depending rather upon the quality than on the quantity of the food. There is a sensation of great tightness which if unrelieved may become acute pain from which the patient obtains ease by bending the body forward, by flexing the right thigh on the abdomen, or by loosening all garments which fit tightly to the waist. There is frequently great complaint of 'acidity' or heartburn, and in the act of belching there may be sour or acid regurgitation. While the discomfort lasts the patient may notice a 'catch' in his breath and he finds, perhaps, that it is impossible to breathe deeply without feeling an acute stabbing pain at the right costal margin. There may be a feeling of faintness and nausea, and, rarely, vomiting may occur spontaneously. After a more than usually severe attack of 'indigestion' the body and side may feel stiff for several days. A frequent and characteristic early symptom is the occurrence, during an attack of indigestion, of a slight sensation of chilliness, especially in the evenings after a meal. The sensation of 'goose-flesh' is often experienced."

*Gall-stone colic* usually develops suddenly with severe, often agonizing, pain in the right hypochondrium or the epigastrium, radiating around

<sup>1</sup> *Brit. Med. Jour.*, Lond., 1913, i, 8.

the chest or to the right scapular region; with nausea, vomiting, and prostration—weak, pulse, rapid heart action, profuse perspiration, etc. Sometimes the attack is preceded by less acute, local pain or discomfort, chilliness, fever, etc.; more commonly (60 per cent. or more of the cases) chilliness and fever accompany and follow the pain. In some cases the severe pain lasts for a few moments only; usually it lasts for from two to twelve hours; in unusual cases it may last much longer, but in these circumstances the phenomena are more correctly interpreted as a succession of paroxysms. Often the pain ceases as suddenly as it began, but, usually following the agonizing pain, more or less dull aching continues for a variable period. The sudden cessation of the severe pain may be interpreted as a sudden relief of tension to which the gall-bladder has been subjected, due to opening of the cystic duct by the dropping of an obstructing gall-stone into the gall-bladder or the passage of the stone from the common duct into the intestine; in this event the calculus may subsequently be found in the stools. The stools should always be searched for calculi by softening them in water or a carbolic acid solution, and passing them through a sieve.

In the great majority if not in all cases local examination reveals tenderness, abdominal rigidity, and the other local phenomena of acute cholecystitis. The colic may recur at varying intervals—days, weeks, months, or years; occasionally there is only one attack; usually there are many; with succeeding attacks the likelihood of other attacks increases.

The pains of cholelithiasis may be colicky or non-colicky. Although there is some discussion as to the cause of the colicky pain, there is little or no objection to attributing the non-colicky pain to inflammatory phenomena provoked by infection, inflammation of and about the gall-bladder and biliary ducts. The dull, aching pains are with excellent reason ascribed to inflammatory changes in the gall-bladder, with the exudation of inflammatory products and consequent distension. The more acute pains, associated with muscular rigidity, tenderness, etc., are due to infection of the regional peritoneum, which as it subsides occasions peritoneal adhesions, a contributing factor in the dull, aching pains, and of other significance. Some considerable distension of the gall-bladder is possible without provoking noteworthy pain, provided the cystic and the common ducts are patulous. It is to efficient drainage that the comparatively symptomless course of some cases of cholelithiasis is to be attributed, although the absence of inflammatory phenomena in the wall of the gall-bladder and the ducts, and the absence of adhesions, are also of significance. As regards the referred pains, although the sympathetic nerve is of significance, the demonstration that filaments of the pneumogastric nerve are distributed to the gall-bladder serves to explain the common association of gastric and cardiac symptoms with disease of the biliary tract; and the frequent occurrence of pain, sometimes of actual colic, three or four hours after a meal, suggests a causal relationship to the normal physiological contraction of the gall-bladder induced by the entrance of the chyme into the intestine.

As regards the colicky pains, there is no doubt that heretofore we have been too much concerned with interpreting them as evidence of the

passage of a gall-stone through the biliary ducts; pains of like character may doubtless be due to different factors, which have been described by Riedel, who gives the following as the causes of gall-stone colic: (1) Adhesions of a gall-bladder no longer containing stones; (2) adhesions when large stones are present in the gall-bladder and the cystic duct is patent; (3) inflammatory processes in a gall-bladder distended by fluid or stones, when the cystic duct is occluded by inflammation or by the presence of a stone in the neck of the gall-bladder; (4) the transit of a stone through the bile passages; and (5) the inflammation of a dilated common duct or its tributaries without impaction of the stone.

There can be little doubt that in a number of cases the spasmodic efforts of the gall-bladder and the common duct to expel their contents by vigorous contraction of their muscular coats are the cause of the peculiar gall-stone colic. This pain occurs in its greatest intensity during the transit of a stone through the ducts, and it ceases as the stone is discharged into the intestine or drops back into the gall-bladder—thus freeing the cystic duct. But there also can be little doubt that attacks of pain indistinguishable from those provoked by the transit of a stone may be due to other factors—those mentioned above; although in some instances the attacks of pain may not be so severe as those of a so-called true gall-stone colic. If the obstruction be incomplete, hypertrophy of the muscular coat results, and later often lessening of the size of the cavity; whereas, if the obstruction be complete, paresis of the muscular coat soon occurs, dilatation ensues, and the pain subsides. But, as exemplified by the 216 patients already mentioned, gall-stones are absent in 15.5 per cent. of the patients who have colicky pains, and they are present in 77.7 per cent. of the patients who have only non-colicky pains.

Furthermore, as is well known, gall-stones may be passed by the bowel; that is, they may ulcerate into the bowel, forming a fistula, without colicky pains having ever been experienced by the patient. As regards the cause of the colic, although mechanical factors, such as traumatism, joltings, etc., may sometimes be the immediately provoking factor, it results in the great majority of cases from infection and consequent inflammation; that is, cholecystitis provokes activity by giving rise to an inflammatory exudation that distends the gall-bladder, which, becoming tense, contracts upon its contents in an effort to expel them, and, should a stone be present, drives it into the neck of the gall-bladder and perhaps into the cystic duct.

Cases of protracted colic may be looked upon as due to long-sustained efforts of the gall-bladder to overcome the obstruction to the egress of its contents, or to slow progress of a calculus along the ducts, the consequence of the large size of the stone or the spiral arrangement of the Heisterian valve which retards progress. Gall-stone colic, therefore, although it is often due to the passage of a gall-stone along the ducts, should be interpreted rather as evidence of acute cholecystitis (or acute exacerbation of chronic cholecystitis): an interpretation sustained by the concomitant occurrence of enlargement and tenderness of the gall-bladder, fever, chilliness, leukocytosis, etc.—the ordinary signs of acute



cholecystitis. Furthermore, as the inflammation subsides the stones become quiescent and the symptoms subside.

*Jaundice* is a common but not a necessary symptom of cholelithiasis, and when it occurs, may come on a variable time after the pain—a few hours or several days; that is, when the obstruction has reached the common duct. It varies in degree and duration with the local conditions. If the obstruction results from the traumatism and consequent catarrh due to the passage of a stone it may be moderate in grade and pass off within a week or thereabouts—as the catarrhal swelling subsides and the duct becomes again patulous. Should the obstruction be more complete and the stone not be discharged, the jaundice may become quite extreme and lasting; but a very large stone may be in the common duct without causing jaundice.

The jaundice of cholelithiasis is mechanical or obstructive and may be due to (1) gall-stones in the hepatic or the common bile duct; (2) spasm of the musculature or inflammatory swelling of the mucosa of the biliary ducts; and (3) compression of the common duct or of the extrahepatic part of the hepatic duct by a large stone in the cystic duct, swollen lymph glands, regional tumors, inflammatory exudations, adhesions, kinking of the ducts, etc. We may, therefore, speak of a lithogenous jaundice, an inflammatory or infectious jaundice, and a compression jaundice—ill-advised as these terms may be on some occasions. The practical deductions to be drawn from the known facts are: (1) That in some cases of cholelithiasis jaundice is not due to obstruction of the ducts by a stone but rather to infection, inflammatory swelling of the ducts, and (2) that in many cases of cholelithiasis jaundice does not occur at all, although other important and distressing symptoms may be quite obtrusive. Of 216 patients, 74 (34.2 per cent.) never had jaundice; 141 (65.3 per cent.) had no jaundice at the time of operation; whereas 121 (56 per cent.) gave a history of attacks of jaundice prior to the time of operation. These attacks, in some cases, antedated the operation many years; in some cases long periods of freedom from jaundice followed; in some cases there were no subsequent attacks of jaundice whatever. Moynihan finds that 25 per cent. of the patients from whose common ducts stones are removed have never been jaundiced.

The *gall-bladder* may or may not be enlarged and palpable. Thus, of 216 patients, in 88 (40.7 per cent.) the gall-bladder was enlarged; in 9 (4.1 per cent.) the gall-bladder was normal in size; in 32 (15 per cent.) the gall-bladder was small and atrophic; and in 87 (40.2 per cent.) the size of the gall-bladder is not known.

Special consideration has been given to the diagnostic importance of the size of the gall-bladder since a knowledge of what is known as Courvoisier's law has become general. Courvoisier, basing his opinion upon an analysis of 187 cases, stated that in cases of chronic jaundice contraction of the gall-bladder is suggestive of gall-stones, and that dilatation of the gall-bladder is suggestive of biliary obstruction caused by factors other than gall-stones—that is, pressure from without, most often carcinoma of the head of the pancreas. This so-called law serves well in the majority of cases, although as Courvoisier himself admitted

there are some notable exceptions. It is of some interest to know that in at least 40.5 per cent. of 116 patients who had gall-stones and jaundice the gall-bladder was enlarged. In somewhat more than one-half of these cases, however, the gall-stones were present in the gall-bladder alone, and the associated jaundice was doubtless due to inflammatory swelling, pressure from without, etc. Courvoisier's explanation of the shrinkage of the gall-bladder in these cases is correct; that is, it is due to inflammatory thickening and cicatrization, the consequence of repeated infection. This process requires time—whence the condition of the gall-bladder varies early and late in the disease. That such cicatrization does occur is suggested by its presence in a number of cases in which gall-stones were present without jaundice. It is manifestly impossible that such a thickened and cicatrized gall-bladder should dilate, no matter what the obstruction in the common duct. One can conceive, however, of an acute cholecystitis or empyema of the gall-bladder (with distension) and an acute impaction of a stone in the common duct (with jaundice); or of hydrops or empyema of the gall-bladder (with distension) and a large stone in the cystic duct compressing the common duct (with jaundice); or of the association of a stone in the common duct and carcinoma of the head of the pancreas, in which event the gall-bladder might be dilated, or small, thickened, and atrophic or sclerosed.

Sometimes when the gall-bladder contains several stones and its walls are not too tense, gall-stone *crepitus* may be elicited by palpation. This is valuable diagnostically when the symptoms are not frank.

As already stated, *fever* is common in cholelithiasis. Of 216 patients, 143 (66.2 per cent.) had fever some time during the course of the disease; 65 (30.1 per cent.) had no fever while under observation; and in 8 (3.7 per cent.) there is no note of the presence or absence of fever. This fever should be correctly interpreted; it is a manifestation of infection, and is not due merely to reflex causes, nervous perturbations, etc., as was at one time thought. In many cases, concurrently with the development of the gall-stone colic, there is a sudden elevation of the temperature, followed sometimes by an equally sudden fall; the onset of this fever may or may not be associated with chilliness or a definite chill; in other cases the fever is of somewhat longer duration, and is more or less obviously due to an acute cholecystitis or an acute exacerbation of chronic cholecystitis; in other cases the fever is slight and not detected unless diligently searched for, perhaps it is sometimes absent—evidently cases of chronic low-grade infection; in other cases, especially cases of calculus in the common bile duct, the fever is that known as Charcot's intermittent hepatic fever—periodic attacks of chill, fever ( $103^{\circ}$  to  $104^{\circ}$ ), and sweats, accompanied by pain, recurrence or increase of jaundice, and perhaps nausea and vomiting. This fever is only an aggravation of the types previously mentioned; all are due to biliary infections.

**Obstruction of the Cystic Duct.**—The calculus is usually lodged in the beginning of the duct or in the termination of the neck of the gall-bladder. The following conditions may ensue: (1) Acute cholecystitis (catarrhal, suppurative, phlegmonous, or gangrenous). (2) Chronic dilatation of the gall-bladder, a condition that follows complete obstruction to the

entrance of bile into the gall-bladder, which soon becomes distended with mucus, at first bile-stained, but ultimately quite clear. The gall-bladder content is perhaps partly inflammatory, in the beginning at least, but in many cases the infection gradually subsides, whereas in others it becomes relighted or a new infection and acute cholecystitis ensue. (3) Chronic fibrous or atrophic cholecystitis—the usual sequel of hydrops when the obstruction is not complete and the infection dies out. The gall-bladder gradually becomes reduced in size and may ultimately be reduced to a mass of fibrous tissue, which usually tightly encircles a calculus. When the gall-bladder becomes small and contracted, symptoms may be in abeyance, or they may be those of chronic cholecystitis with or without acute exacerbations, or those of adhesions. Often there is incrustation of the wall with cholesterin; there may be diverticula which usually contain calculi.

**Obstruction of the Common Bile Duct.**—There may be one or many obstructing calculi; in the majority of cases there is only one, and this is usually in the lower end of the common duct or the diverticulum of Vater, but it may be in any part of the duct; when there are many calculi they may extend throughout the common duct into the hepatic duct and its branches and into the cystic duct and the gall-bladder. The obstruction may be complete or incomplete, and may or may not be associated with cholangitis. When the obstruction is complete a stone is usually tightly impacted in the common duct; when the obstruction is incomplete the stone may be more or less fixed, but permits the flow of bile around it, or it may circulate in the common duct and imitate the conditions in a ball valve. A calculus originally tightly impacted in the common duct often, in the course of time, becomes more or less free, in consequence of atrophy or ulceration of the wall of the duct about the stone, or of dilatation of the duct above the stone. Dilatation of the ducts is a common event; it is usually cylindrical, the common duct not infrequently becoming as large or larger than one's finger; occasionally the dilatation is saccular, the common duct attaining the size of an orange; small saccular dilatations may also occur on the surface of the liver, especially the left lobe. The liver at first is usually somewhat enlarged from accumulation of bile; later atrophy of the hepatic cells ensues, and in consequence of biliary infection, inflammatory phenomena spread from the bile ducts to the adjacent tissue—cholangitis and pericholangitis. This gives rise to some new connective tissue, and the atrophy of the hepatic parenchyma causes a relative increase in the preëxisting connective tissue, so that a condition resembling cirrhosis is induced; but although a form of chronic hepatitis, this is not cirrhosis and it is at best doubtful if biliary stasis can lead to true cirrhosis.

The *clinical* manifestations of a stone in the common duct vary, depending whether the obstruction is complete or incomplete and whether or not it is associated with infection of the ducts. In the event of complete obstruction without infection, permanent and lasting jaundice is produced, unattended by fever and other signs of local infection. In the event of incomplete obstruction suggestive symptoms are sometimes absent, as a large stone may be present for years without jaundice.



Usually, jaundice is present; it lasts a long time, and, varying with the degree of biliary obstruction, is subject to more or less fluctuation, which is very characteristic; and there is fever, periodic, intermittent, remittent, or more or less continuous, indicative of the concomitant biliary infection. This biliary infection is present in practically all cases of incomplete obstruction; it may continue for years without the advent of suppuration, but suppurative cholangitis and cholecystitis may ensue.

Naunyn gives the following as the characteristic signs of a calculus in the common bile duct: "The continuous or occasional presence of bile in the feces; distinct variations in the intensity of the jaundice; normal size or only slight enlargement of the liver; absence of distension of the gall-bladder; enlargement of the spleen; absence of ascites; presence of febrile disturbances, and duration of the jaundice for more than a year." Osler has emphasized the importance of the following signs in the diagnosis of a ball-valve calculus in the diverticulum of Vater (where it occurs most frequently), or in the common bile duct: "(a) Ague-like paroxysms of chill, fever, and sweating—the hepatic intermittent fever of Charcot; (b) jaundice of varying intensity, which persists for months or even years, and deepens after each paroxysm; and (c) at the time of the paroxysm, pain in the region of the liver with gastric disturbance.

. . . Pain, which is sometimes severe and colicky, does not always occur. There may be vomiting and nausea. As a rule, there is no progressive deterioration of health. In the intervals between the attacks the temperature is normal."

When the calculus is situated in the diverticulum of Vater it may obstruct the duct of Wirsung, and should the duct of Santorini be unable, on account of non-communication, to divert the pancreatic juice into the duodenum, accumulation of the juice and dilatation of the ducts ensue; furthermore, the common infection present in these cases gradually spreads to the pancreatic ducts, producing *pancreatitis*, with early enlargement of the organ, especially the head, which may become so hard as to suggest carcinoma; later the organ becomes contracted and fibrosed; in some cases pancreatic lithiasis also ensues. Mayo<sup>1</sup> states that in 2200 operations upon the gall-bladder and biliary ducts the pancreas was found coincidentally affected 141 times (6.1 per cent.); since the total number of operations undertaken for disease of the pancreas was only 168, it was found that 81 per cent. of the cases were due to or accompanied by gall-stones. In 268 operations upon the common and the hepatic ducts the pancreas was found diseased in 18.6 per cent., as contrasted with 4.45 per cent. of the cases in which the gall-bladder only was diseased.<sup>2</sup> In the event of incomplete obstruction of the pancreatic duct, bile may be diverted into it, and lead to the production of acute hemorrhagic pancreatitis.

**Complications and Sequelæ.**—Of the many complications and sequelæ of cholelithiasis, some infectious, some purely mechanical, but most of them infectious and mechanical, the following are the most important:

<sup>1</sup> *Jour. Am. Med. Assoc.*, 1908, i, 1161.

<sup>2</sup> Consult also Mayo Robson, *Surg. Gynecol. and Obstet.*, 1908, vi, 29; and Maugeret, *Cholecysto-pancréatite*, Paris, 1908.

(1) Infectious (inflammatory) lesions of the biliary tract and adjacent viscera; (2) chronic pericholecystic adhesions; (3) biliary fistulæ; and (4) intestinal obstruction.

**Infectious (Inflammatory) Lesions of the Biliary Tract and Adjacent Viscera.**—It has been demonstrated that gall-stones are the consequence of infective (low-grade) inflammation of the biliary tract. Having been formed, gall-stones participate in a vicious circle and serve to keep alive the infective inflammation to which they owe their origin, in consequence of which and also on account of certain mechanical effects, divers inflammatory lesions of the biliary tract and adjacent viscera ensue. These comprise especially varying grades of acute and chronic, suppurative and non-suppurative, cholangitis and cholecystitis, progressing perhaps to ulceration, gangrene, perforation, etc., to which reference has already been made. The inflammatory phenomena may extend to adjacent structures and set up peritonitis, pylephlebitis, pancreatitis, etc., or, in consequence of adhesions, they may seriously compromise the functional activity of the gastro-intestinal tract; or progressing to necrosis and suppuration they may lead eventually to the formation of fistulæ.

**Chronic Pericholecystic Adhesions.**—Adhesions are frequently encountered in the upper abdomen; of 216 patients, 123 (56.6 per cent.) had adhesions about the gall-bladder; 22 (10.1 per cent.) had no adhesions; and of 71 (33 per cent.) there is no note of the presence or absence of adhesions (probably none were present). These adhesions represent the sequels of past subacute and chronic, sometimes acute, inflammation of the organs of the upper abdomen, of which the biliary tract is the chief; whence they are a direct result of biliary infection.

The conditions are quite analogous to those in and about the vermiform appendix. Should the biliary infection be acute and virulent, the bacteria or their toxins penetrate the wall of the gall-bladder or the biliary ducts and engender a fibrinous exudation, a more or less local peritonitis. In the subacute and chronic infections, however, the formation of adhesions goes on less obtrusively, often entirely latently, whence the symptoms that develop later are commonly misinterpreted. In consequence of milder infections the less virulent toxins give rise to less inflammatory phenomena—sufficient, however, often to lead to more or less widespread adhesions. All gradations are encountered; frequently these are quite localized and very delicate (gall-spiders, resembling spider-webs, they have been aptly called by Morris); in other cases they are quite widespread and very dense.

The clinical recognition of these adhesions is sometimes a matter of difficulty, but it is perhaps not impossible in the majority of cases. It is essential, in the first place, that we recognize that many of the cases of so-called “stomach-ache,” “biliousness,” indigestion, etc., in reality have an anatomical basis. Many of these cases are due to an unsuspected or latent gastric or duodenal ulcer, definite cholecystitis, chronic pancreatitis, etc.; in other cases they are due to adhesions. We must study attentively patients who complain of general ill health, with more or less ill-defined gastric or epigastric symptoms. Attacks of such symptoms may come on periodically without definite cause; they may last a few

days, and cease quite as causelessly. Now and then the attack may be ushered in with chilliness (rarely a definite chill), and may be attended by a little fever. Examination may reveal some tenderness in the epigastrium, perhaps a little to the right of the median line, toward the region of the pylorus or the gall-bladder, and some rigidity of the overlying muscle. Deep pressure is sometimes very painful. Later, should the pylorus or the duodenum become obstructed, the commoner manifestations of dilatation of the stomach supervene. Special diagnostic importance attaches to intractability of the symptoms and a history of past infection of the biliary tract. In the event of suspecting such adhesions, we must exclude other factors that may cause similar symptoms, remembering that in many cases symptoms supposedly due to disease of the stomach or intestine are due to disease of the gall-bladder or adhesions of the upper abdomen. Much has been accomplished in the study of these adhesions by means of the x-ray.

**Biliary Fistulæ.**—Fistulous communications between the biliary tracts and adjacent viscera as well as the exterior of the body frequently result from cholelithiasis and the associated inflammatory and ulcerative processes. Courvoisier in a study of 499 cases found that fistulous communications had been established as follows: between different parts of the biliary passages in 8; into the portal vein in 5; into the peritoneal cavity in 70; into peritoneal adhesion in 49; into the retroperitoneum in 3; with the stomach in 13; with the duodenum in 83; with the jejunum in 1; with the ileum in 1; with the colon in 39; with the urinary tract in 7; with the pleura and lung in 24; and externally in 196. The external fistulæ appear to be disproportionately numerous since by their very nature they command attention, whereas the internal fistulæ frequently are not detected. In external fistulæ the opening may be near the normal situation of the gall-bladder, near the umbilicus (being directed thither by the falciform ligament), in the right iliac fossa, in the thigh, etc. Biliary, gastric and intestinal fistulæ are often unsuspected; sometimes they are first revealed by the discharge of gall-stones with the feces (without concomitant gallstone colic), or by the sudden disappearance of long-standing obstructive jaundice, or by the onset of intestinal obstruction (gall-stone ileus). Bronchobiliary fistulæ lead to cough, dyspnoea, and the expectoration of pus, bile, and perhaps gall-stones. Schlesinger<sup>1</sup> and Eichler<sup>2</sup> have added to the cases and there are now 47 cases on record, of which 28 were due to gall-stones.

**Intestinal Obstruction.**—Intestinal obstruction is a rather rare event that may follow ulceration of a gall-stone from the gall-bladder into the duodenum or, less commonly, the colon. It is doubtful if a gallstone that has been able to pass through the biliary ducts and the ampulla of Vater into the duodenum is large enough to obstruct the intestine; in some cases a comparatively small stone may become arrested at the ileocecal valve; it may set up inflammation and localized spasm of the intestine with consequent obstruction; it may become increased in size after it reaches the intestine (enterolith); or it may become arrested in

<sup>1</sup> *Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, Jena, 1906, xvi, 240.

<sup>2</sup> *Ibid.*, 1906, xvi, 550.



a part of the intestine narrowed by inflammatory or neoplastic disease, etc. The ratio of gall-stone ileus to other forms of intestinal obstruction varies between 1 to 13 (Fitz) and 1 to 45 (Barnard). Recently, Lesk<sup>1</sup> has collected 148 cases, of which 109 (73.5 per cent.) occurred in women and 39 (26.5 per cent.) in men. Only 6 of the patients were less than forty years of age; most of them were beyond fifty. In 104 of Lesk's cases the obstruction was in the ileum in 62 (59.6 per cent.), in the jejunum in 17 (16.3 per cent.), in the small intestine (without definite statement) in 13 (12.5 per cent.), in the colon in 6 (5.7 per cent.), in the duodenum in 5 (4.8 per cent.), and in the rectum in 1 (1 per cent.). In 26 of the 62 cases in which the obstruction was in the ileum it was near the ileocecal valve. The diagnosis rests upon the advanced age of the patient and a past history of gall-stones or other manifestations of biliary infection; in some cases the gall-stone causing the obstruction and the surrounding or adjacent tissues form a palpable mass in which the gall-stone may be distinguishable. In most cases, however, the cause of the intestinal obstruction cannot be diagnosed with certainty until it is seen. Sometimes the obstruction is relieved spontaneously, but at least one-half of the patients die unless the obstruction is relieved by surgical procedures. The operative mortality is high (about 45 per cent.), due largely to delay, but also to the advanced age of the subjects.

**Diagnosis.**—This comprises the recognition of the gall-stone colic and of the many and varied associated lesions and sequels. Severe pain in the epigastrium or the right hypochondrium, radiating around the chest or to the right scapula, accompanied by nausea and vomiting and enlargement and tenderness of the gall-bladder, and followed by jaundice and the detection of a gall-stone in the feces, are characteristic of the passage of a gall-stone; but jaundice is by no means always present and the other symptoms may be provoked by cholecystitis in the absence of a gall-stone; indeed, with increasing experience it becomes often more and more difficult to say whether or not gall-stones are present in certain cases of obvious chronic biliary infections.

Recourse to the *x*-rays is seldom of much diagnostic utility, since the cholesterin stones produce scarcely any shadow, usually not more than the adjacent liver; in the rare cases of calcium stones more shadow is cast, but this also is obscured by the shadow of the liver. In a few cases, however, the *x*-rays afford trustworthy evidence.

A diagnosis after the event is readily made in many cases, but during the prevalence of the severe pain one may be unable to determine the cause of the patient's suffering. A few whiffs of chloroform or a hypodermic injection of morphine may so relieve the patient as to permit of an examination, in which event tenderness and perhaps enlargement of the gall-bladder may be elicited. The severe pain of gall-stone colic may be imitated by renal colic or intestinal colic; but in renal colic the pain is usually in the back, loin, or groin, and radiates down the ureter to the testicle, which may become retracted; strangury or frequent micturition is common; the kidney is usually tender (the tenderness being in the

<sup>1</sup> *Deutsche Ztschr. f. Chir.*, Leipz., 1908, xcix, 47.

loin rather than anteriorly in the region of the gall-bladder); and the urine subsequently contains blood and a proportionate amount of albumin, perhaps crystals or a calculus, and pus and epithelium from the pelvis of the kidney; and it does not contain bile. Intestinal colic is usually due to some more or less obvious cause; the pain is usually about the umbilicus, it radiates in different directions, remits and intermits, and subsides with the removal of the exciting cause, often with belching or the discharge of feces or gas or mucus by the bowel; and there is no localized tenderness in the region of the gall-bladder. In lead colic there is the history of exposure to the poison, a blue line on the gums, anemia, basophilic degeneration of the erythrocytes, etc.

When the symptoms, especially the pain, are less acute, and do not merit the designation gall-stone colic, difficulty may be experienced in differentiating disorders of the stomach. Much assistance will be obtained by bearing in mind that the case of so-called chronic indigestion that is not benefited by several months of well-directed therapy commonly has an anatomical basis. Gastric or duodenal ulcer is suggested by dependence of pain upon taking food or its occurrence as the chyme passes into the duodenum (which sometimes obtains also in cholelithiasis), by tenderness in the median line or slightly to the right, and posteriorly on the left side near the vertebræ, hyperchlorhydria, hematemesis, etc., and the absence of jaundice and intermittent hepatic fever; prominence of nausea and vomiting is more significant of cholelithiasis. Pericholecystitis and perigastric adhesions are often the cause of so-called chronic indigestion, and may give rise to pyloric obstruction and gastric dilatation.

Malignant disease of the gall-bladder usually follows cholelithiasis, but so insidious, as a rule, is its onset that it is commonly not suspected until the advent of loss of flesh and strength and the progressive development of cachexia. In some cases of more or less apparent cholelithiasis the diagnosis of carcinoma is favored by the detection of progressive nodular enlargement of the gall-bladder, and the progress of the disease is shown in some cases by the occurrence of metastasis to the liver, ascites, etc. In the event of jaundice, its persistence unchanged suggests malignant disease of the ducts or pancreas, etc., although it may be due to a stone tightly impacted in the common duct; but there is less impairment of the general health than in carcinoma; in the majority of cases of gall-stones in the ducts, as contrasted with malignant disease or catarrhal cholangitis, there is periodic variation in the intensity of the jaundice and fever (intermittent hepatic fever).

**Prognosis.**—The prognosis, as a rule, depends more upon the associated conditions than upon the mere presence of the gall-stones. The prognosis in gall-stone colic is virtually that of a more or less acute cholecystitis; the outlook as regards permanent health depends upon the chronic gall-bladder infection. In almost all cases of gall-stone colic the acute symptoms subside spontaneously after several hours or several days; rarely a patient may die, it is said, from shock and cardiac failure; occasionally rupture of the gall-bladder ensues and gives rise to infectious peritonitis and a fatal issue; and in other cases a stone impacted in the

neck of the gall-bladder or the cystic duct and the attendant infection and interference with the blood-supply may, after the lapse of several days, lead to severe suppurative or gangrenous cholecystitis.

A first gall-stone colic is sometimes the last and the infection subsides. Usually, however, there are subsequent attacks, if not of severe colic, of more or less disturbance with digestion, and general impairment of health, due to the toxic absorption, etc.; some subjects pass into chronic invalidism from unrecognized chronic biliary infections. The likelihood of continuation of symptoms is increased by the duration of symptoms in the past; that is, those already ill for some time are likely to continue ill, and the lesions to progress. The detection of faceted stones in the feces suggests that other stones are still undischarged; the detection of rounded or ovoid stones in the feces, together with subsidence of the local symptoms, arouses the hope that there was but a single stone. The occurrence of intermittent hepatic fever, especially of severe ague-like paroxysms, renders the prognosis rather bad, since it shows active infection, which, although it may persist for years without suppuration, may nevertheless lead to serious consequences. The prognosis as to final recovery of health is bad in pericholecystic adhesions, fistulæ, and intestinal obstruction without operative intervention.

**Treatment.**—The intelligent treatment of cholelithiasis presupposes a clear conception of (1) the pathology of the disease, of its pathogenesis, pathological anatomy, and natural tendencies, and (2) of the means of treatment at our command and the objects attainable by their use. To attempt by internal medication to dissolve a gall-stone that is insoluble; to cause the passage through the biliary ducts of a gallstone when the ducts are impassable to a stone of its size; to attempt to cure supposed gastric symptoms by measures directed to the stomach when the cause of the symptoms is adhesions about the gall-bladder, and to cause the solution of these adhesions—is as futile as it is irrational.

**Prophylaxis.**—A knowledge of the etiology suggests certain measures of prophylaxis. Although we may be quite unable to prevent the causative infection in the individual, we may advise useful measures. The fact that gall-stones are most common in women, in the obese, in those who lead a sedentary life, eat too much, are constipated, and addicted to alcohol, suggests the correction of certain very obvious etiological factors. Women who have been repeatedly pregnant and have lax abdominal walls should wear proper supports; but women, whether they have been pregnant or not, should avoid tight lacing. Men and women who lead a sedentary life should take properly regulated exercise; they should practise deep breathing (to promote the movements of the diaphragm), bathe frequently, be much in the open air, etc.; that is, they should apply to themselves the general principles of hygienic living. Constipation should be overcome, and the diet should be such as will be presently pointed out. If these measures do not prevent the formation of gallstones in those who have or have had a biliary infection, they will at least promote a general well being, tend to reduce biliary infection, and perhaps obviate some of the serious consequences of cholelithiasis.

When gall-stones have formed, the main indications for treatment are:



(1) To cause solution of the stone or stones; (2) to cause the discharge of the stone or stones; and (3) to treat the complicating infection.

*Solution of the Gall-stones.*—As regards the solubility of the gall-stones Naunyn<sup>1</sup> states that we have to consider cholesterin, bilirubin-calcium, calcium carbonate, and calcium phosphate. Of these, bilirubin-calcium and the inorganic salts of calcium are insoluble in the bile; cholesterin, however, is quite soluble in the bile, and even in conditions of disease the bile scarcely if ever contains so much cholesterin that it cannot take more in solution. We have, therefore, to admit the possibility of cholesterin stones being dissolved. In fact, there is some experimental evidence that goes to prove that not only *in vitro*, but also *in vivo*, cholesterin stones may be dissolved. Naunyn quotes Labes' experiments of thirty years ago, in which he introduced gall-stones into the gall-bladder of dogs, and, killing the animals two months later, found that partial solution of the stones had occurred. Bain<sup>2</sup> and von Hansemann<sup>3</sup> have published the results of studies that show the same possibility. In these experiments, however, the calculi were introduced into normal gall-bladders (or, as in one or two of Bain's experiments, into gall-bladders in which a cholecystitis has been artificially produced). The conditions are quite different in the human subject affected with gall-stones and it is exceedingly doubtful whether spontaneous solution of gall-stones ever occurs in the human subject—indeed, whether it is at all possible.

Judging from clinical experience, it is exceedingly doubtful whether, with any means at our command, we can cause solution of gall-stones in the gall-bladder. We now know that the thousands of gall-stones said to have been passed by the bowel after the administration of olive oil are merely masses resembling gall-stones in outward appearance (saponified oleic acid). There is also no reason to believe that olive oil, derivatives of olive oil and other oils, turpentine, ether, etc., have any influence whatever in dissolving gall-stones in the biliary tract.

*Discharge of the Gall-stones.*—This is an occurrence which should not be hoped for nor awaited or sought by medical means, even were such at our command; it cannot be considered an object of rational treatment.

*Treatment of the Biliary Infection.*—The one worthy object is to restore the latency from which the gall-stones have been awakened—in other words, to control the infection at the basis of gall-stone activity. This must also be the object of medicinal or internal treatment of cholecystitis in the absence of gall-stones. The infection of the biliary tract is what the physician has to treat. The surgeon may remove the stones and also treat the biliary infection. The physician, however, in many cases may lead his patient into a condition of virtual cure, that is, latency or sterility of the biliary tract; but he must recognize his limitations, and not subject his patient too long to useless treatment when early surgical intervention may restore him to health. The

<sup>1</sup> *Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, Jena, 1905, xiv, 537.

<sup>2</sup> *Brit. Med. Jour.*, 1905, ii, 269.

<sup>3</sup> *Arch. f. path. Anat.* (etc.), Berl., 1913, cexii, 1.

manifestations of the biliary infection calling for treatment may be acute, that is, gall-stone colic, or chronic.

The *pain of gall-stone colic* is usually so severe as to require the administration of morphine, which not only relieves the pain (and mitigates the attendant shock) but, by relaxing the spasm of the biliary musculature, favors the exit of bile from the tense gall-bladder and the transit of the calculus through the ducts (if it be already therein). A few whiffs of chloroform or ether will usually carry the patient through the painful period until the morphine has time to act; or, and this is often attended with excellent results, an additional dose of atropine ( $\frac{1}{100}$  grain) may be administered hypodermically.

The use of coal-tar products for the relief of the pain is ill advised, since not only are they comparatively inefficacious but they also add to the depression of an already depressed patient; the salicylates and olive oil (even when tolerated) also are of no value during the acute stage, although olive oil by inducing vomiting may assist in dislodging the stone. Sometimes it may relieve an associated hyperchlorhydria.

In many cases relief may also be afforded by hot fomentations over the region of the gall-bladder and by lavage of the stomach with water as hot as can well be borne. All food should be withheld during the continuance of the acute symptoms; indeed, the nausea and vomiting lead the patient usually to decline food. Vomiting ceases with the cessation of the pain, so that the best treatment for the vomiting is that which tends to relieve the pain and the lesions upon which it is founded. Should the vomiting persist and be manifest especially by ineffectual retching, resort should be had to lavage: if it has not been previously used, sodium bicarbonate may be added to the hot water. A hot bath may also be resorted to at the very beginning of the attack, with hope of excellent result. In other cases the vomiting may be relieved by bismuth, carbolic acid, sips of hot water and brandy, champagne, etc. In some cases the pain leads to extraordinary depression of the patient, which, if it is not relieved by the morphine, should be met with whisky or brandy in hot water, or the hypodermic use of camphor.

Upon the subsidence of the pain, as well as in the absence of a definite gall-stone colic, the medical treatment is that of the chronic biliary infection. By promoting the flow of bile one may effect the discharge of infecting bacteria and their toxins from the biliary passages and prevent their ascent to the smaller ducts, and by the constant irrigation thus produced, as well as by other measures, one may allay the inflammatory phenomena. Ultimately, the biliary tract may be rendered sterile, and should the inflammatory phenomena subside completely a condition of latency, quiescence of the gall-stones, results. In rare cases this latency is permanent, and the patient experiences no further complaints. In most cases a low-grade chronic catarrh of the gall-bladder persists; in other cases the gall-bladder readily again becomes infected, and the patient in consequence is continuously or intermittently ill. Should gall-stones be passed by the bowel, one must remember that all the gall-stones harbored by the patient are seldom, if ever, thus passed,

and that even were this the case, the persisting catarrh of the gall-bladder is quite certain to give rise to the formation of new stones.

The *diet* should be carefully regulated. In character and amount it should be such as may be readily digested, and not overtax the resources of the liver and promote congestion; and the time intervals between meals should be such as tend to frequent and free emptying of the gall-bladder. Cholelithitic subjects should have a sufficient but not an excessive diet; in character it should be based less upon the mere presence of gall-stones than upon the attendant gastro-intestinal catarrh, constipation, and jaundice (if present). In general a mixed diet is the best; this should contain considerable and varied protein, which is believed to promote an abundant supply of bile acids and to stimulate the flow of the bile. In the presence of jaundice, proteins and readily digested carbohydrates should be advised, and the fats should be much reduced or excluded for a time, since they are ill digested in the absence of bile; but in the absence of jaundice it is unnecessary to prohibit fat on the mistaken apprehension that a fatty diet tends to increase the cholesterin in the bile. Naunyn has said that a full meal is an excellent cholagogue, so that with the hope of preventing stagnation of the bile an additional meal may be given at bedtime, unless in some way contra-indicated. In most cases it is wise to prohibit the use of alcohol.

The utility of large amounts of water, especially of alkaline mineral waters containing sodium salts, is unquestionable. Since they have no solvent action on the gall-stones, and do not influence the alkalinity of the bile, their beneficial effect is probably on the associated biliary and gastro-intestinal catarrh. There is some experimental evidence that these waters do not directly stimulate the flow of bile, and that the excessive amount of fluid does not dilute the bile, but this doubtless results indirectly, the removal of biliary constituents from the intestine leading to renewed formation; and an insufficient supply of water tends to inspissation and stagnation of the bile.

The treatment can often be best carried out at one of the well-known spas, but equally good results may be obtained at the patient's home although they are unlikely. Of Carlsbad or similar water, from a half pint to a pint should be taken hot on an empty stomach half to one hour before breakfast, and a similar amount in the middle of the afternoon; in some cases the best results follow smaller amounts half an hour before each meal and on retiring at night. It is wise to begin with small doses and gradually increase; the amount and the frequency of administration should be gauged by the result, particular attention being paid to free evacuation of the bowels. The saline cathartics, magnesium or sodium phosphate, may be used instead of the natural waters. The effect on the bowels may be enhanced by large injections of hot or cold water.

Many drugs have been advocated in the treatment of cholelithiasis from time to time, but few have withstood the test of experience. Cholagogue properties have been ascribed to many that need not be mentioned; salicylic acid and its preparations and preparations of the bile itself are efficacious. Salicylic acid seems to augment the flow of bile by stimulating its production, and since it also possesses antiseptic



properties and is excreted with the bile, it exerts a most desirable influence on the biliary infection. No preparation is better than chemically pure salicylic acid; it may be combined with sodium bicarbonate or sodium benzoate; or the salicylates or other preparations of salicylic acid may be given. Crowe<sup>1</sup> demonstrated that hexamethylenamine is excreted in the bile and the pancreatic juice, directly through the wall of the gall-bladder, etc., and that, especially after single large doses (75 grains within twenty-four hours), it appears in the bile in such amount as to exert a decided bactericidal action. Ox-gall also stimulates the secretion and outpouring of bile, and thus favors drainage of the biliary tract; it should be administered as salts of the bile acids, such as sodium glycocholate (10 to 15 grains daily). Ammonium chloride also is sometimes extolled for its effect upon inflamed mucous membranes; by promoting the free flow of thin bile it may assist in flushing the biliary tract.

**Surgical Treatment.**—In many cases medication is altogether inefficient, and resort must be had to surgical intervention. The important question to decide is, When should an operation be undertaken? The writer is by no means prepared to say that the diagnosis brings with it the indication for surgical intervention. In many cases the question of early operation scarcely admits of discussion. These are cases in which there is acute cholecystitis (with or without cholangitis—jaundice), with evidences of severe infection, and in which the symptoms and local signs, instead of abating, become more pronounced: these comprise cases of acute cholecystitis developing during or after an attack of typhoid fever, as well as during the course of previously latent or manifest cholelithiasis, and in which impending if not actual infection of the hepatic ducts is not unlikely. The risk attending the progress of the disease in such cases is more than the hazard of the operation; indeed, without operation many would unquestionably soon terminate fatally. Happily, however, most of the acute infections of the biliary tract subside spontaneously or under treatment. In general, it is much wiser that the acute manifestations should subside without operation—which, should it be deemed desirable later, may then be undertaken with much more reasonable hope of ultimate success.

Immediate operation is imperative also in the event of acute intestinal obstruction in a cholelithitic subject, or in a person in whom adhesions have been suspected. Operation, although not always necessarily immediate, is indicated in all cases of persistently enlarged gall-bladder, whether due to simple hydrops, empyema, or gall-stones.

The question of when to operate in cases of gall-stones that have become or have been active must be decided in each individual case; but one should bear in mind that, as a rule, it is not the many stones in the gall-bladder that do the most damage, but the one or two stones that get into the ducts, that the special risk attending operations for gall-stones increases with delay, and that whereas gall-stones are readily removed from the gall-bladder, their removal from the ducts is commonly attended with serious difficulties and is sometimes impossible. The

<sup>1</sup> *Johns Hopkins Hosp. Bull.*, 1908, xix, 109.

time of election for operation, therefore, is before the stones have entered the ducts. This is by no means always possible, or, indeed, desirable. Thus one should not advise the removal of stones that are and always have been quiescent. If, however, the gall-bladder is enlarged and the stones have given warnings—local discomfort and distress—operation should be undertaken. Nor would the writer insist upon operation after a single short successful gall-stone colic (so-called), but he would by no means be averse to it. Two, certainly three, attacks should be looked upon as a positive indication for operative intervention. In the event of hesitation on the part of the patient, the pathological changes and the likely course of the disease should be explained, and he should be required to make the decision for or against operation.

In impaction of a gall-stone with chronic jaundice operation is called for; personal conviction is for early rather than delayed intervention. The risk of gall-stone operations is the risk of delay, since with delay serious infections of the biliary tract supervene, the tendency to pronounced hemorrhage increases with the persistence of the jaundice, the general nutrition of the patient fails, he becomes less able to withstand the vicissitudes of the operation, and stagnation of the bile leads to dilatation of the ducts and seriously compromises the functional activity of the liver cells. The decision as to the time of operation must be made for each individual patient, but there scarcely seems any advantage attending a delay beyond one or two weeks, and this, too, in full knowledge of the fact that some patients have recovered without operation after a much longer period. Finally, operation is indicated in those obscure cases in which with reasonable certainty the presence of pericholecystic, perigastric, or periduodenal adhesions may be surmised.

In each of the foregoing classes of cases operative measures attain that which is impossible of attainment, or attainable only with difficulty by medicinal measures—whence surgical measures find their justification. They find additional justification in the fact that early intervention tends to prevent the development of certain complications and sequelæ. An operation, however, should not be lightly undertaken in persons suffering with disorders of nutrition, or in those with faulty kidneys, etc. The risk attending the operation is too great and the recuperative power of the patient too much reduced to expect from operation a great deal more than can probably be attained by well-directed medicinal, hygienic, and dietetic treatment, aside from the fact that in the one instance the patient will remain alive, although indisposed, while in the other he may be much longer dead. Finally, the fact that the operative results are not always what were hoped for is not in itself a contra-indication to operation; on the contrary, these untoward results are often attributable rather to the fact that in many long-delayed cases the anatomical lesions are such as to be almost if not quite irremediable by any and all means at our command.

## CARCINOMA OF THE GALL-BLADDER AND BILIARY DUCTS

Carcinoma of the gall-bladder and biliary ducts may be primary or secondary. The secondary cases are of comparative rarity and of little clinical importance; usually the lesions constitute a subordinate part of a general carcinomatosis. The metastases in the gall-bladder consist of nodules of varying size, rarely of a more diffuse infiltration on or just beneath the peritoneum; the mucosa is seldom involved. The biliary ducts are much less rarely implicated, although occasionally invaded from without in carcinoma of the pancreas, stomach, etc. These secondary growths form usually only an insignificant part of the general metastasis, and can scarcely be recognized clinically, unless the irregular, nodular enlargement of the gall-bladder becomes conspicuous, or the cystic or common bile duct becomes obstructed. In the first of these two events hydrops of the gall-bladder may ensue, and in the other, chronic jaundice, which only with difficulty can be distinguished from other types of chronic jaundice.

*Primary carcinoma* of the gall-bladder and the biliary ducts is a tolerably frequent disorder—three to four times as common in the gall-bladder as in the biliary ducts. At the necropsy it is often difficult to determine definitely where the lesion began, but it seems desirable to exclude from the cases of primary carcinoma of the biliary ducts those in which the new growth developed from the fine intrahepatic ducts; these are virtually cases of carcinoma of the liver. When the extrahepatic ducts are involved, the disease may spread along the ducts and involve the gall-bladder, the pancreas, the omentum, etc., or primary disease in any of these structures may spread to the ducts. Thus carcinoma of the gall-bladder and of the cystic duct is virtually one disease, although sometimes it may be differentiated; carcinoma of the gall-bladder and of the pancreas may spread to the biliary ducts, and *vice versa*; carcinoma of the gastrohepatic omentum may originate in the biliary ducts; and in some cases so widespread is the new growth and so dense and cicatricial the adhesions that carcinoma, if at all suspected, can only with the greatest difficulty be referred to its true point of origin. In some cases the condition is thought to be inflammatory, and only a microscopic examination will disclose its real nature. With care, however, most cases can be correctly interpreted. Rare cases of sarcoma of the gall-bladder and biliary ducts have been described.

**Etiology.**—*Primary carcinoma of the gall-bladder* is a fairly common disease. In 1889 Musser<sup>1</sup> collected 100 cases; in 1901 Fütterer<sup>2</sup> collected 268 cases. The disease is much more common in women than in men; in Musser's cases there were 75 females to 23 males (3 to 1); in Fütterer's, 204 females to 52 males (4 to 1). It is especially prevalent in advanced life; the average age in Fütterer's cases was fifty-eight years. An important etiological question is the interpretation of the relationship between carcinoma of the gall-bladder and cholelithiasis. Frequently they are

<sup>1</sup> *Boston Med. and Surg. Jour.*, 1889, cxxi, 525, 553, 581.

<sup>2</sup> *Ueber die Aetiologie des Carcinoms*, 1901.



associated: in 69 per cent. of the cases (Musser), in 78 per cent. (Fütterer), in 81 per cent. (Winton), in 85 per cent. (Zenker), in 91 per cent. (Courvoisier), in 95 per cent. (Siegert), and in 100 per cent. (Janowski). Rolleston, from a study of many statistics, estimates that carcinoma of the gall-bladder occurs in from 4 to 14 per cent. of cases of cholelithiasis. At 262 operations on the gall-bladder and biliary ducts done by Dr. Deaver, carcinoma was found in 6, of which 5 had also gall-stones.

*Carcinoma of the extrahepatic biliary ducts* has been attentively studied by Rolleston, who has collected 90 cases. Of 85 of these, 50 (58.8 per cent.) occurred in males and 35 (41.1 per cent.) in females. In 58 (69.8 per cent.) of 83 cases the patient was beyond fifty years of age; extremes of age were eight-one years (a woman) and twenty-nine years (a man). In contrast with carcinoma of the gall-bladder, gall-stones are much less frequently associated with carcinoma of the biliary ducts; in 67 of Rolleston's cases, gall-stones were present in 23 (34.3 per cent.).

*Carcinoma of the ampulla of Vater* (choledochopancreatic duct) also has been studied by Rolleston, who has collected 19 cases; of these, 14 were in males and 5 in females; the average age was 55.2 years in both sexes, the extremes being thirty-four and eighty-one years. Since gall-stones were present in only 2 of the 19 cases, it is likely, as Rolleston maintains, that there is no relationship between gall-stones and carcinoma of the ampulla of Vater.

**Pathology.**—*Carcinoma of the gall-bladder* most commonly involves the fundus, which is said to be due to the fact that, being the most dependent part, the fundus is especially subject to irritation by a gall-stone; second in point of frequency of growth is the neck of the gall-bladder or the beginning of the cystic duct—attributed to the attrition of impacted gall-stones; third, the growth may be situated anywhere in the gall-bladder or involve the entire organ. In 45 of Fütterer's cases the growth was situated at the fundus in 17, at the neck in 13, in the posterior wall in 8, and on the anterior wall in 7. Two types of growth may be distinguished: that which projects into the lumen, a villous or cauliflower-like growth, and is believed by some to originate as a papilloma, and that which infiltrates the wall of the gall-bladder, and is believed by some to originate as an adenoma. In reality the two varieties cannot be differentiated; the one growth may exhibit appearances significant of both types. Extension to the liver ensues in more than 50 per cent. from direct growth into the adjacent liver, or by extension along the biliary ducts, by way of the lymphatics in the wall, or through the lumen of the ducts. Adhesions between the carcinomatous gall-bladder and adjacent organs are common.

In the 90 cases of *carcinoma of the biliary ducts* collected by Rolleston the situation of the growth was as follows: In the common bile duct, 34 (lower end 23, midpart 11); at the junction of the common bile duct, cystic duct, and common hepatic duct, 27; in the common hepatic duct, 19; in the right or left hepatic ducts, 3 (the last two classes constitute the so-called juxtahepatic cases); in the cystic duct, 6; and in the cystic duct and the lower end of the bile duct, 1. Usually the growth infiltrates the wall of the duct and forms a firm annular stricture; occasionally it

extends in the wall of the ducts for a considerable extent, and transforms them into thick rigid tubes; in some instances the growth projects considerably into the lumen, and produces obstruction rather than annular stricture. Complete biliary obstruction is produced, due in part probably to added muscular spasm, since after death the stricture does not always appear to be absolutely impervious.

Above the growth the biliary ducts are dilated, sometimes to such an extreme degree as to allow a finger or a thumb to be introduced. When the growth is in the common bile duct the gall-bladder is distended, except it be bound down and retracted on itself in consequence of former cholelithiasis; when the growth is in the common hepatic duct, the gall-bladder is nearly always small, except in the rare instances in which it may be distended with mucus from concomitant obstruction of the cystic duct, or may be occupied by a number of gall-stones; when the growth is situated at the junction of the cystic, hepatic, and common bile ducts, the gall-bladder, as a rule, is not enlarged, but from irregularities and variations in the degree of obstruction to the different ducts, corresponding differences in the gall-bladder are met with.

The liver, in addition to dilatation of the biliary ducts, reveals atrophy of the parenchymatous cells, focal necrosis, relative increase in the connective tissue, and in the event of chronic infection of the biliary ducts pericholangitic fibrosis, but no true cirrhosis; suppurative lesions may follow acute infections. Usually the growth does not invade adjacent tissues or organs, but it may grow into the pancreas, liver, or portal vein (and cause portal thrombosis). Metastases are uncommon, largely because of speedy death; they are most common in the liver (13 of 57 of Rolleston's cases); but they occur also in the regional lymphatic glands, the peritoneum (causing ascites), etc.

*Carcinoma of the ampulla of Vater* (choleodochopancreatic duct) should be distinguished from carcinoma of the termination of the common bile duct, of the termination of Wirsung's duct, and of the duodenal surface of the biliary capillaries. The growth tends to obstruct the orifice of Wirsung's duct and thus to produce dilatation of the intrapancreatic ducts and chronic interstitial pancreatitis; the same result may ensue upon extension to the orifice of Wirsung's duct of carcinoma of the lower end of the common bile duct.

**Symptoms.**—The onset of the symptoms referable to *carcinoma of the gall-bladder* may or may not be preceded by symptoms due to associated disease—cholecystitis and cholelithiasis. Some patients complain for years of what is commonly called dyspepsia, but which careful inquiry would show to be in reality chronic cholecystitis with perhaps pericholecystic adhesions; in other cases there is a more or less clear history of antecedent gall-stones. There may have been many and recent attacks of obvious colic (with or without jaundice), or there may have been few, perhaps only one, remote and ill-defined attacks; that is, as perhaps occurs in most cases, the gall-stones have remained latent.

The onset of the symptoms referable to the carcinoma is insidious, and usually the disorder makes considerable progress before its true nature is suspected. The patient, usually an elderly woman, complains

of ill-defined gastric symptoms, associated with more or less severe, sometimes colicky, pain. These are usually ascribed to dietetic indiscretions; in some cases, however, the pain is so severe and perhaps referred to the right of the median line, and some local tenderness is found on examination, that the symptoms are put down to cholecystitis or cholelithiasis. The attack subsides, perhaps it recurs; the patient is thought to be the subject of cholelithiasis, and, indeed, in most cases, for some time the symptoms may be quite indistinguishable from cholecystitis with pericholecystic adhesions.

Soon, however, the gall-bladder enlarges, jaundice supervenes, or the general health becomes impaired. An obvious palpable and often visible enlargement of the gall-bladder develops in more than half of the cases; in itself it is not significant of carcinoma, since it resembles that due to cholelithiasis or obstruction of the cystic duct; in advanced stages, however, it may become quite irregular and nodular, whereupon it is much more significant of new growth. Usually it reveals its attachment to the liver by moving with it during the phases of respiration and showing no intervening area of tympany; sometimes it is fixed to the abdominal wall by adhesions, and it may be quite tender. In some cases the tumor is the first obtrusive evidence of the disease.

*Jaundice* occurs in three-fourths or more of the cases (69 per cent., Musser; 86 per cent., Meurrier); but it is not always due to the same cause. Rarely it may result from duodenal catarrh or catarrhal cholangitis, last a short time and subside; or it may be due to a gall-stone in the common biliary duct, when it is likely to be intermittent and perhaps accompanied by intermittent fever; usually, however, it is due to extension of the new growth into the biliary ducts, or to pressure from without on the extrahepatic biliary ducts. The jaundice in this event is progressive, soon becoming very deep, and it is permanent.

With the progress of the disease the general health becomes impaired; this may be the first noteworthy evidence of its malignant nature. The patient gradually loses weight and strength, becomes anemic, and presents the manifestations of cachexia. Dyspeptic symptoms develop, or become aggravated, in which event they may be due only not to the original cholecystitis or cholelithiasis, but also to an associated pyloric obstruction. Occasionally the carcinoma may invade the colon, giving rise to obstruction, or to a cholecystocolonic fistula. In other cases the gall-bladder forms adhesions with the peritoneum, and ultimately perhaps perforates thereinto, giving rise to a localized or more generalized peritonitis. *Ascites* occurs in about one-fourth of the cases, and is due most commonly to associated perihepatitis or peritonitis; rarely it may be due to obstruction of the portal circulation by the original growth or secondarily involved glands. Ultimately in the cases with jaundice the patient develops a condition attributed to hepatic insufficiency (hepatic toxemia, cholemia) and dies with asthenia, delirium, and coma. In the absence of jaundice, the patient generally dies of asthenia. The disorder may run a fatal course within six months.

The symptoms of *carcinoma of the extrahepatic biliary ducts* are usually insidious. There may be antecedent dyspeptic symptoms of variable



duration, and ill-defined complaints of disturbance of the general health. Jaundice is usually the first noteworthy symptom. In most cases it develops gradually; occasionally rather suddenly, imitating catarrhal cholangitis or a gall-stone arrested in the common duct. The jaundice is progressive and permanent; it soon becomes extreme, and biliary coloring matter disappears from the stools and appears in the urine. Pain in the right hypochondrium or the epigastrium is quite common, and is usually dull in character; sometimes it is severe, suggesting gall-stone colic, but it is more likely due to spasmodic contraction of the gall-bladder against an obstruction. Obstruction to the flow of bile results in enlargement of the gall-bladder, which is palpable in one-half or more of the cases as a smooth pear-shaped swelling. Metastasis occurs in about one-half of the cases, but the nodules are usually small and not palpable during life. Should metastasis occur, it may lead to ascites. Infection of the biliary ducts and suppurative cholangitis may ensue. The symptoms of *carcinoma of the ampulla of Vater* are practically identical with those of carcinoma of the common bile ducts.

**Diagnosis.**—Carcinoma of the gall-bladder is suggested by a history of ill-defined dyspeptic symptoms, perhaps interrupted by definite signs attributable to cholelithiasis or cholecystitis; pain in the right hypochondrium; jaundice; hard, nodular, and progressive enlargement of the gall-bladder; and gradual loss of flesh and strength. Attention to the sequence and grouping of the symptoms would probably permit of the diagnosis before the onset of jaundice, which is not a phenomenon of carcinoma of the gall-bladder itself, but of extension of the disease; but in the great majority of cases jaundice supervenes before the patient is thought to be seriously ill. Carcinoma of the biliary ducts is suggested by insidious but persistent and progressive jaundice, smooth, uniform enlargement of the gall-bladder, loss of flesh and strength, in a patient about or over fifty years of age, without determinable cause of jaundice.

Carcinoma of the gall-bladder and biliary ducts is simulated by a number of other conditions, such as chronic cholecystitis and cholelithiasis, carcinoma and other tumors of adjacent organs. Chronic cholecystitis and cholelithiasis are, in most cases, antecedent to carcinoma of the gall-bladder, so that it is extremely difficult if not impossible, in most cases, to say when the new growth begins. The diagnosis is favored by the detection of progressive nodular enlargement of the gall-bladder; but in many cases the carcinoma develops when the chronic inflammatory process has lasted a long time and caused much thickening and many adhesions to adjacent viscera, so that should the growth not attain at least moderate dimensions, no specially noteworthy enlargement of the gall-bladder becomes apparent. The diagnosis in these cases awaits the development of cachexia, or of metastasis, especially to the liver. Obviously then the diagnosis is often impossible until the disease has progressed so far as to be hopeless.

In the early stages, carcinoma of the gall-bladder may sometimes be distinguished from carcinoma of the liver, by the absence of jaundice, due to limitation of the new growth to the gall-bladder; but in the more advanced stages, when the disease is more widespread and involves

the liver more or less extensively, the diagnosis may be quite impossible, although a history of antecedent cholelithiasis or cholecystitis, and the early development of a tumor in the region of the gall-bladder without jaundice, suggests that the primary growth originated in the gall-bladder; while antecedent gastric, intestinal, genital, etc., symptoms, jaundice, and the early absence of a tumor in the region of the gall-bladder, suggest that the liver rather than the gall-bladder was originally involved.

Carcinoma of the head of the pancreas, causing jaundice, can scarcely, if ever, be distinguished from carcinoma of the biliary ducts, aside from the fact that carcinoma of the head of the pancreas is much more common, the pain is more likely to be epigastric than hypochondriac; a tumor deep in the epigastrium (close to the vertebræ) may sometimes be felt.

In the early stages, carcinoma of the gall-bladder and of the biliary ducts may sometimes be distinguished by the absence of jaundice and the presence of an enlarged and nodular gall-bladder, and the early presence of jaundice and a smooth and uniform enlargement of the gall-bladder. Later, when jaundice occurs in carcinoma of the gall-bladder, the jaundice being due to extension to the ducts or pressure by enlarged glands on the ducts, the differences are slight.

Carcinoma of the ampulla of Vater closely resembles carcinoma of the biliary ducts. Rolleston states that there are a few points of difference: in carcinoma of the ampulla (1) jaundice is said to be often intermittent, the feces becoming bile-stained, and the icteric tint of the skin diminishing or even passing off in the earlier stages when the obstruction is possibly valvular, or partly due to spasm of the ducts set up by the irritation of the growth. Confusion is apt to arise between carcinoma of the ampulla and carcinoma of the duodenal surface of the papilla, in which jaundice is by no means constant; (2) intermittent hepatic fever and suppurative cholangitis are apt to occur; (3) diarrhœa is more often seen than in carcinoma of the ducts. Attacks of diarrhœa may alternate with periods of obstinate constipation (Rolleston).

**Prognosis.**—Carcinoma of the gall-bladder and the biliary ducts is necessarily fatal, unless it can be removed by surgical intervention. Under non-surgical treatment patients seldom live more than six months from the onset of serious symptoms. The mortality is high also under surgical treatment, many patients succumbing to the operation or to postoperative hemorrhage; in others the growth is too extensive to be removed; in others, recurrences ensue or a fistula persists.

**Treatment.**—The treatment is essentially surgical. Since there is no known means of cure at the hands of the physician, his energies should be directed toward making an early diagnosis and urging surgical intervention. Even the suspicion of malignant disease is an indication for operation; the hazard of the operation is less than the risks attendant upon delay. Since carcinomas occur in from 4 to 14 per cent. of cholelithic subjects, the operative treatment of cholelithiasis naturally tends to reduce the incidence of carcinoma of the gall-bladder. Aside from the removal of the growth, a fistula may be established between the gall-bladder and the intestine in cases of carcinoma of the common duct or of the ampulla of Vater. Aside from operation, the physician's efforts are limited to relieving distress and promoting comfort.

## CHAPTER VIII

### DISEASES OF THE PANCREAS

By EUGENE L. OPIE, M.D.

#### GENERAL PATHOLOGY AND SYMPTOMS

ALTHOUGH the pancreas is essential to the normal digestion of proteins, carbohydrates, and fats, and controls the assimilation of carbohydrates, in only a small proportion of cases does disturbance of these functions indicate with certainty disease of the organ. Evidence of disturbed function is obtainable only when the gland is the seat of advanced disease. Complete extirpation of the gland in animals is followed both by glycosuria and by changes in the digestion of proteins and fats; partial extirpation may be unaccompanied by glycosuria or by disturbances of digestion, since a small part of the gland has been found to fulfil both the internal or metabolic and the external or secretory function of the gland. The impairment of function resulting from slight injury may be unrecognizable under ordinary conditions, and demonstrable only by special means which tax the capabilities of the organ. Moreover, complete occlusion of the duct of Wirsung, which is usually the larger duct of the gland, does not necessarily prevent access of the secretion to the intestine, since the duct of Santorini, anastomosing with it, may be large enough to act as an outlet for the entire secretion.

**Symptoms Due to Impairment of Pancreatic Secretions.**—These concern (1) the external secretion of the gland, indicated by disturbance of digestion or by the effects of retained secretion, and (2) the internal function of the organ, causing disturbance of carbohydrate metabolism. Since the pancreatic juice contains ferments which are concerned in the digestion of proteins, fats, and carbohydrates, impaired absorption of these constituents of the food may follow destruction of the secreting parenchyma or such occlusion of the ducts that pancreatic juice no longer enters the duodenum.

Incomplete digestion of various elements of the food in association with pancreatic disease is indicated by passage of voluminous feces first noted by Oser. Schmidt<sup>1</sup> has determined the weight of the dried feces in individuals receiving a test diet and has found that it may be doubled in patients with pancreatic disease. Pratt<sup>2</sup> has made similar observations and has shown that separation of the pancreas from the duodenum may double the weight of the dried feces in dogs receiving a uniform diet.

**Steatorrhœa.**—Although this has been regarded by Friedreich and other writers as a symptom of much diagnostic value, they recognized

<sup>1</sup> Test Diet in Intestinal Disease (Trans.), Philadelphia, 1906.

<sup>2</sup> *Amer. Jour. Med. Sc.*, 1912, cxliii, 313.



the fact that it accompanies only a small proportion of even grave pancreatic disorders. Finding jaundice associated with cases of pancreatic disease, in which steatorrhœa indicated impaired absorption of fat, Fr. Müller has attributed the symptom to obstruction of the common bile duct. A review of recorded instances of steatorrhœa with pancreatic disease, made by Fitz<sup>1</sup> in 1903, does not confirm this view, but establishes the diagnostic value of the symptom in the relatively small number of cases in which it occurs. He was able to collect from the literature 29 cases in which autopsy, laparotomy, or the passage of a pancreatic calculus gave evidence of disease of the gland, and in only 12 of these cases was jaundice found. In the 17 cases in which jaundice was absent the lesion of the pancreas was in 7 cases tumor, usually cancer; in 6 cases calculi within the ducts; in 2 cases cysts with atrophy; in 2 instances the lesion was designated fatty degeneration. In a case with symptoms of obstruction of the pancreatic ducts and no jaundice, studied by Pratt and Morrison, 58.9 per cent. of the fat of the food reappeared in the feces, whereas in normal individuals not more than 5 to 10 per cent. of fat is lost.

In the recorded cases the character of the feces has varied considerably. In some instances superficial examination demonstrates the presence of free fat, which is described as oily or like butter, while in other cases the feces are described as gray, silvery gray, or asbestos-like. The fat, which is liquid when passed, may solidify on cooling and form a layer covering the fecal mass. The presence of fat recognizable by the eye constitutes a true steatorrhœa.

In the uniform metallic-gray or asbestos-like stools sometimes seen, the abnormal fatty contents are demonstrated with greater certainty by chemical methods which may show the amount of neutral fat, fatty acids, and soaps. Such fatty stools may occur in normal individuals who have ingested fat in quantity so great that the normal limit of absorption has been exceeded. Ability to digest and absorb fat is diminished, according to Nothnagel, when bile fails to enter the intestine, when absorption is hindered by certain diseases of the intestine or its lymphatic apparatus—namely, amyloid disease, extensive atrophy of the mucous membrane, caseation of the mesenteric lymphatic glands, and tuberculous peritonitis, or when very active peristalsis prevents the normal action of the digestive juices.

Although Müller found in 2 cases of pancreatic disease no increase in the percentage of fecal fat, chemical analysis demonstrated a diminution of split fat. In health, according to his observations, the unabsorbed fecal fats consist of approximately from 20 to 30 per cent. of neutral fat and from 70 to 80 per cent. of split fat, which is partly fatty acids and partly soaps. In his two cases the split fat was diminished to 22.4 and 47.7 per cent. respectively. In some cases of pancreatic disease access of pancreatic juice in considerable amounts to the intestine, even though the duct is partially occluded or the parenchyma partially destroyed, may explain the absence of diminished splitting of fat. Katz<sup>2</sup>

<sup>1</sup> *Transactions of the Congress of American Physicians and Surgeons*, 1903, vi, 36.

<sup>2</sup> *Wiener med. Woch.*, 1899, xlix, 153.

has maintained that diminution of fatty acids and soaps below 70 per cent. of the total amount of fecal fat indicates diminished action of the pancreatic juice, and only in nursing infants and in patients with profuse diarrhoea is the diagnostic significance of this condition lost. Fitz has collected from the literature 11 cases of pancreatic disease, confirmed by autopsy, in which analyses of the fecal fat had been made during life; in 7 instances jaundice was absent. The total amount of fat determined in 4 instances was slightly increased, but in no case apparently was there macroscopic steatorrhoea. The percentage of neutral fat in 7 instances of uncomplicated disease of the pancreas was normal or less than normal in only 1 case, and although the results have not been constant, a well-marked diminution in the proportion of split fat has been usually present in such cases.

Macroscopic or chemical evidence of diminished digestion and absorption of fat, obtained by examination of the feces, indicates the presence of pancreatic disease when other disturbing influences, such as jaundice or intestinal diseases preventing absorption or hastening peristalsis, can be excluded. In the absence of macroscopic fat in the feces, demonstration of diminished splitting of fat by chemical examination may suggest the presence of pancreatic disease. With the data at present available little significance can be attached to the proportion of fatty acids to soaps, although Zoja<sup>1</sup> found diminution of the latter with pancreatic disease.

The capacity of different individuals to digest fat varies within such wide limits that little information concerning impaired power of digestion can be obtained by observing the effect upon the feces of the administration of a fixed amount of fat. Hartsen found no increase of fecal fat after administration of from eight to ten teaspoonfuls of cod-liver oil to two diabetics, in each of whom autopsy showed advanced atrophy of the pancreas.

By administering fresh pancreas to animals from which the pancreas has been removed the consequent impairment of fat absorption has been diminished. Abelman found that the pancreas of the pig fed to a dog, the pancreas of which had been extirpated, caused a decrease in the amount of undigested fat and of protein as well in the feces. Similar observations have been made by other experimenters, and are confirmed by a few observations made upon patients with pancreatic disease. Fles, quoted by Friedreich, records the case of a man suffering with diabetes mellitus who passed undigested meat and fat in such quantities with the feces that it could be separated by ounces. A part of the milky fluid obtained by rubbing in a mortar half of the fresh pancreas of a calf with six ounces of water and straining the mixture was administered after each meal in such quantity that one pancreas was consumed daily. At the end of two days all fat had disappeared from the feces and the number of undigested fibres of striped muscle was greatly diminished. Whenever the administration of the infusion was discontinued, fat and muscle fibres reappeared in the feces. The condition of the patient

<sup>1</sup> Quoted by Oser, *Die Deutsche Klinik*, 1901, v, 151.

improved for a time, but diabetes mellitus persisted, and death occurred as the result of tuberculosis. Advanced sclerosis of the pancreas was found at autopsy. In a patient with jaundice and suspected cancer of the pancreas Oser observed improved digestion of fats following the administration of one gram of pancreatin (Merck) taken daily in divided doses. Tileston<sup>1</sup> has collected the published cases in which the effect of pancreas or pancreatic preparations upon absorption has been studied in patients with pancreatic disease and has found that loss of both fat and nitrogen may be decreased.

Little is known concerning the effect of continued steatorrhœa upon nutrition and health. Walker has described the case of a man who for twenty years passed large colorless stools of putrid odor, containing free oily or solid fat. There was no jaundice. During this time he was in good health and engaged in the practice of medicine; there was no marked emaciation. He died at the age of ninety years. The pancreas was apparently replaced almost wholly by fat, and its duct was occluded by an irregular calculus situated about an inch from the duodenum.

**Azotorrhœa.**—The presence of undigested protein material in the feces, so-called azotorrhœa, has been less frequently observed in association with pancreatic disease than disturbed digestion of fat. After causing almost complete destruction of the pancreas in dogs, Claude Bernard found undigested muscle fibres and even large pieces of meat in the feces. Abelman found that less than 2 per cent. of the nitrogen of the food reappears in the feces of normal dogs; when the pancreas is completely removed, 56 per cent. of ingested nitrogen was lost with the feces, whereas after partial removal 46 per cent. was lost. When the pancreas of the pig was administered, loss of nitrogenous material was diminished to approximately 24 per cent. Other observers have obtained similar results. In a case described by Wientraub autopsy demonstrated advanced chronic interstitial pancreatitis; in the feces during life he recovered 45.2 per cent. of the ingested protein and only 22.2 per cent. of the fat taken as food. He suggests that pancreatic disease causes as great disturbance of the digestion of proteins as of fats, perhaps an even greater disturbance, and is therefore distinguishable from intestinal disturbances such as amyloid disease, caseation of the mesenteric lymph glands, etc., which hinder absorption of fat alone. With closure of the duct of Wirsung by carcinoma, Zoja recovered from the feces nitrogenous material equal in amount to 70 per cent. of that taken in the food. In patient with obstruction of the pancreatic ducts Pratt and Morrison recovered 50.9 per cent. of nitrogen.

The presence of undigested meat in the feces may give indication of disturbed protein digestion. Fles found well-preserved muscle fibres in the feces of the patient previously mentioned, and administration of an extract made from the pancreas of a calf caused their disappearance. Fitz collected from the literature only 8 cases in which the presence of undigested muscle fibres in the feces had been associated with clearly demonstrated pancreatic disease; in 5 of these cases steatorrhœa was

<sup>1</sup> *Trans. Assoc. Amer. Phys.*, 1911, xxvi, 537.



present. The condition, as he pointed out, probably occurs only when there is extreme diminution of the pancreatic juice, and is significant only when gastric digestion is normal, when the diet contains no excess of meat, and where there is no diarrhœa.

The *persistence of nuclei in remnants of muscle fibres passed with the feces* has been proposed by Adolph Schmidt as a test of the efficiency of pancreatic digestion. He maintains that the nuclear material of meat can be digested only by the pancreatic juice, and the presence of nuclei in muscle fibres expelled with the feces indicates defective pancreatic secretion. The test has no value if the cubes remain in the intestine less than six or more than thirty hours, for putrefaction may destroy the nuclei. Kashiwado<sup>1</sup> has isolated the nuclei of the thymus by gastric digestion and stained them with hematoxylin; 0.5 gram of a powder composed of equal parts of partially digested thymus and lycopodium are administered in capsules. The nuclei, if undigested, are recognized in the feces.

Beef muscle failed to lose its nuclei when passed through the intestinal canal of three dogs from which the pancreas had been removed; Pratt has confirmed this observation. Steele<sup>2</sup> found the test little more than an index of proteolytic digestion in the intestine, giving only vague information concerning the pancreatic secretion.

With methods for demonstrating the presence of trypsin in the feces by digestion of the surface of serum agar plates (Edw. Müller and Schlect) or of casein (Gross) the attempt has been made to test the activity of pancreatic secretion. Boldyreff and later Volhard have demonstrated that regurgitation of trypsin into the stomach may be brought about by administration of olive oil, and Einhorn<sup>3</sup> has devised a method which permits removal by intubation of duodenal contents. Absence of trypsin with these procedures has been regarded as evidence of impairment of pancreatic function. Methods of measuring the activity of diastatic enzymes in the feces have been employed with the same end in view.

Since end-products of pancreatic digestion are readily attacked by bacteria, impairment of pancreatic excretion has been believed to diminish the amount of ethereal sulphates in the urine (Rosenberg). Edsall<sup>4</sup> thinks that diminution of ethereal sulphates in the urine should suggest pancreatic disease when conditions are present which usually cause their increase. He recognizes, however, that ethereal sulphates may be diminished with a variety of diseases which do not affect the pancreas. In favor of his opinion he cites a case of carcinoma of the pancreas, demonstrated by autopsy, and the cases of LeNobel and of Taylor, in which the same lesion was probably present.

By applying the phenylhydrazine test for sugar to urine previously boiled with strong hydrochloric acid, Cammidge<sup>5</sup> has obtained sheaves of yellow crystals which he believes indicate pancreatic disease.

<sup>1</sup> *Deutsch. Arch. f. klin. Med.*, 1911, civ, 584.

<sup>2</sup> *University of Pennsylvania Medical Bulletin*, 1906, xix.

<sup>3</sup> *Jour. Amer. Med. Assn.*, 1910, lv, 6.

<sup>4</sup> *American Journal of the Medical Sciences*, 1901, cxxi, 401.

<sup>5</sup> *British Medical Journal*, 1906, i, 1150.

**Impairment of the Metabolic Function of the Pancreas.**—Glycosuria and diabetes mellitus are so frequently associated with pancreatic disease that it is necessary to consider them among its symptoms and to define the peculiarity of those lesions which cause disturbance of carbohydrate metabolism. The relation of the islands of Langerhans to carbohydrate metabolism has been described in the chapter on Diabetes Mellitus. Study of the histological anatomy of pancreatic disease has furnished data by which it is possible to define the anatomical basis of diabetes mellitus. In 1904 Sauerbeck<sup>1</sup> was able to collect from the literature of the subject 176 cases of diabetes mellitus studied by observers who have given attention to the islands of Langerhans; it has been possible to collect 112 additional cases which have since become available.<sup>2</sup> In some instances different writers have described the same change under different names. For example, the same lesion has been designated atrophy and chronic pancreatitis, and rarely has a distinction been made between atrophy causing diminution in the size of the gland and congenital smallness of the gland. The lesion designated lipomatosis introduces further error, for in some cases it indicates a moderate increase of the interstitial fat, and is a trivial abnormality which is not responsible for the existing glycosuria, whereas in other cases increase of fat is the result of interstitial inflammation, and is accompanied by sclerosis or hyaline degeneration of the islands of Langerhans. From the available records it is often impossible to classify such cases. The findings are as follows:

Interacinar pancreatitis . . . . .	123
Atrophy . . . . .	65
Lipomatosis . . . . .	18
Interlobular pancreatitis with no occlusion of ducts . . . . .	13
Lithiasis . . . . .	9
Cyst . . . . .	1
Carcinoma . . . . .	5
Focal necrosis . . . . .	2
Secreting parenchyma normal or approximately normal:	
Hyaline degeneration of islands of Langerhans . . . . .	6
Sclerosis . . . . .	4
Diminution . . . . .	5
Hypertrophy . . . . .	3
Normal . . . . .	34
	<hr/>
	288

Among 90 cases of diabetes more recently studied by Cecil<sup>3</sup> interacinar pancreatitis which represents the lesion often designated atrophy was present in 63 instances, interlobular pancreatitis in 4 instances; in 12 instances these were lesions of the islands of Langerhans but no changes in the secreting parenchyma, and in 11 instances no pathological changes were found.

Hypertrophy of the islands of Langerhans which has been observed with diabetes mellitus is of two kinds: (1) Simple hypertrophy, which

<sup>1</sup> Lubarsch and Ostertag, *Ergebnisse der allgem. Path.*, 1904, viii, 588.

<sup>2</sup> Opie, *Disease of the Pancreas*, Philadelphia and London, 1910.

<sup>3</sup> *Jour. Exper. Med.*, 1909, xi, 266.

accompanies destructive lesions of these structures (Schmidt, Pearce<sup>1</sup>), and (2) adenoma-like hypertrophy, which may occur in young individuals without other lesions of the islands of Langerhans (Herxheimer, Reitmann, MacCallum<sup>2</sup>). Hypertrophy doubtless occurs because existing islands of Langerhans are insufficient to meet the functional demand.

It is noteworthy that in a considerable number of cases of diabetes no lesion of the pancreas is demonstrable. Experimental and pathological data establish with certainty that diabetes mellitus may be the result of pancreatic disease, and save in a comparatively small percentage of cases this origin is demonstrable. That the islands of Langerhans and secreting parenchyma are normal in a group of cases does not oppose the theory that lesions of the former are responsible when the pancreas is the source of the disease, for it equally opposes any theory of pancreatic diabetes. It is not improbable that complex carbohydrate metabolism may be disturbed by factors which do not concern the pancreas.

The foregoing considerations make it possible to define with greater accuracy the conditions under which glycosuria and other symptoms of diabetes occur as symptoms of pancreatic disease, and to determine the relation which diabetes holds to steatorrhœa, azotorrhœa, and other evidence of an insufficient supply of pancreatic juice. Since sclerosis of the islands of Langerhans or hyaline degeneration of these structures may occur in the presence of little or no change affecting the secreting acini, diabetes may occur without digestive symptoms of pancreatic insufficiency, and indeed, the greater number of cases of pancreatic diabetes belong to this group. Destructive lesions, such as abscess, acute hemorrhagic pancreatitis and diffuse carcinoma invading the gland, destroy equally islands of Langerhans and secreting acini, and in the majority of instances affect a previously healthy gland. The resulting condition resembles that which follows partial extirpation, and is accompanied by diabetes only in the comparatively rare cases in which almost the whole gland is destroyed.

Occlusion of the pancreatic ducts does not cause diabetes, and the resulting chronic interlobular pancreatitis is accompanied by the disease only when it has reached the advanced stage, in which the parenchyma is largely replaced by dense fibrous tissue. When the pancreatic ducts have been occluded by calculi or by new growth, steatorrhœa and perhaps other symptoms of deficiency of pancreatic juice may occur without diabetes; of the 29 cases of steatorrhœa collected by Fitz, in 11 diabetes was present. It is not improbable that the application of chemical methods to the examination of feces would demonstrate insufficiency of pancreatic digestion in a much larger number of instances of duct obstruction at a time when diabetes has not appeared.

Histological studies have explained the relationship of a variety of diseases, such as arteriosclerosis and cirrhosis of the liver, to diabetes mellitus. Grube found arteriosclerosis 66 times among 117 cases of diabetes. Chronic interstitial pancreatitis accompanying sclerosis of the pancreatic vessels has been described; this change which affects

<sup>1</sup> *Albany Medical Annals*, 1904, xxv, 329.

<sup>2</sup> *Amer. Jour. Med. Sci.*, 1907, cxxxiii, 432.



the interacinar tissue of the gland implicates the islands of Langerhans. G. Hoppe-Seyler,<sup>1</sup> who has studied 18 such cases, found a close relation between the severity of the glycosuria and the degree of change affecting the islands of Langerhans. The frequency with which diabetes is caused by disease of the arteries is shown by 112 cases of diabetes which have been recently recorded; in association with general arteriosclerosis there was, in 23 cases, sclerosis of the pancreatic arteries and interacinar pancreatitis; in 26 additional cases there was either general or local arterial sclerosis, in 10 instances with interacinar pancreatitis.

The frequency with which diabetes mellitus accompanies *cirrhosis of the liver* has been explained by the presence of chronic pancreatitis. Numerous studies have shown that conditions which cause cirrhosis of the liver act upon the pancreas and cause chronic inflammation. The literature contains numerous instances of this association, which is well exemplified by the disease known as hemochromatosis; pigmentary cirrhosis of the liver is accompanied by chronic pancreatitis, which invades the islands of Langerhans and causes diabetes (*diabète bronzé*).

That *alimentary glycosuria* demonstrable by the administration of a fixed quantity of sugar may accompany a variety of pancreatic lesions is shown by the investigation of Wille. From 70 to 100 gm. of grape sugar dissolved in half a liter of coffee were administered in the morning before other food had been taken to 800 patients suffering with a great variety of diseases. Subsequently 77 of them came to autopsy. Temporary glycosuria had been produced in 15 of these, and grave lesions of the pancreas were found in 10—namely, chronic interstitial inflammation, or carcinoma of the gland, either primary or secondary to tumors in the stomach, liver, or gall-bladder. Alimentary glycosuria may occur in the absence of pancreatic lesion with a variety of diseases, especially with hysteria and other neuroses, chronic alcoholism, and exophthalmic goitre. Its occurrence, however, may give information when other conditions suggest the presence of pancreatic disease of moderate intensity. Hoppe-Seyler tested the ability of individuals with arteriosclerosis to assimilate 100 gm. of glucose. Alimentary glycosuria was present in 42 per cent. of 62 patients with arteriosclerosis, and was more frequently observed when arteriosclerosis was associated with acute alcoholism.

### FAT NECROSIS

This lesion, characterized by the death of fat cells in sharply circumscribed areas, is frequently associated with disease of the pancreas. By some writers (Balsér) it has been regarded as an often fatal disease accompanied by certain somewhat indefinitely defined symptoms. The lesion when widely disseminated is, in the greater number of instances, the result of acute hemorrhagic pancreatitis. Its recognition is of great importance to the surgeon, since the presence of the characteristic opaque white foci studding the translucent abdominal fat will explain the nature of otherwise obscure conditions.

<sup>1</sup> *Deutsches Arch. f. klin. Med.*, 1904, lxxxi, 119.

**Etiology.**—The inconstant results of bacteriological examinations do not support the opinion of a few observers (Ponfick) who have maintained that the lesion is caused by bacteria. Its relation to bacteria is doubtless that suggested by Welch, who obtained the colon bacillus from foci of fat necrosis in association with hemorrhagic pancreatitis; diphtheritic and ulcerative colitis apparently had facilitated the entrance of *B. coli*, which were found not only in the patches of necrotic fat but in the mesenteric lymph glands, liver, bile, lungs, spleen, and kidneys.

**Experimental Fat Necrosis.**—Studies of R. Langerhans first brought the lesion into relation with the peculiar physiology of the pancreas. He was able to demonstrate that the fat of the necrotic cell is split into fatty acids, which are deposited as needle-like crystals, and glycerin, which is absorbed. The occurrence of the lesion in association with disease of the pancreas, its greatest intensity in the neighborhood of the gland, and the changes demonstrable within the fat cells have suggested the probability that the pancreatic ferments, particularly the fat-splitting ferment, have an important part in its production. Hildebrand and Dittmer subjected the pancreas to a variety of injuries and produced fat necrosis. If the gland were simply cut across, thus allowing the escape of the pancreatic secretion, foci of necrosis were found in the immediate neighborhood of the gland. If penetration of pancreatic secretion into fat tissue is facilitated by transplanting the duodenal part of the pancreas containing the severed ends of the ducts into the subcutaneous fat of the abdominal wall in cats, extensive subcutaneous necrosis of fat is thus produced (Opie). In these experiments conditions have been present which afford an opportunity for the escape of pancreatic secretion into the tissue surrounding the gland. Flexner has demonstrated the presence in the necrotic foci of a ferment capable of splitting neutral butter fat and setting free acids which are recognizable by suitable tests. That the lesion is caused by a ferment is further shown by the experiments of Wells;<sup>1</sup> watery extracts of the pancreas of the hog constantly produce fat necrosis in cats and dogs, but fail to do so when boiled or after heating to a temperature above 71° C. Whether the lesion is wholly due to the action of the fat-splitting ferment or is the result of its action on tissue previously injured by some other constituent of the pancreatic juice, perhaps by the proteolytic ferment, is not yet definitely determined.

**Incidence of Fat Necrosis.**—In human cases extensive fat necrosis is more frequently associated with hemorrhagic and gangrenous pancreatitis than with other lesions of the gland, and constantly accompanies acute hemorrhagic pancreatitis produced experimentally by the introduction of a great variety of irritant substances into the gland. The well-known fact that bile forms a favorable medium for the action of the pancreatic ferments, and particularly of the fat-splitting ferment, the activity of which may be increased by it twofold or threefold, probably explains in part the extent of the lesion accompanying many cases of hemorrhagic pancreatitis which may be caused by the penetration of

<sup>1</sup> *Jour. Med. Research*, 1903, ix, 70.

bile into the pancreas. Fat necrosis has been found with obstruction of the duct of Wirsung caused by pancreatic calculi, by biliary calculi, or by carcinoma invading the head of the pancreas, but in such cases foci of necrosis are not abundantly distributed, nor does the lesion usually follow obstruction of the pancreatic duct. In a small proportion of cases chronic interstitial pancreatitis is accompanied by fat necrosis, which is probably caused by constriction of small branches of the pancreatic duct.

In several cases of extensive fat necrosis no noteworthy lesion of the pancreas has been demonstrable. In such a case described by Fraenkel the lesion was explained by a gall-stone lodged in the diverticulum of Vater, while in a somewhat similar case of Flexner's, gall-stones were present in the common bile duct near its termination. A unique case described by Wulff<sup>1</sup> is not in accord with other observations and with present knowledge of the lesion is unexplainable, unless an incomplete autopsy failed to disclose an aberrant pancreas, biliary calculi, or some cause of duct obstruction.

**Pathological Anatomy.**—A feature of the lesion is its occurrence in sharply defined foci. On opening the abdomen the omentum and perhaps fat in other situations is found to be studded with rounded or oval areas, which vary in diameter from less than one to five or more millimeters. They are very conspicuous, on account of their opaque, white or yellowish color, in sharp contrast with the translucent golden yellow of the fat in which they occur. These areas are not infrequently surrounded by a narrow hemorrhagic zone. Such foci are most numerous upon the peritoneal surface, usually extending only a short distance below it, but also occur embedded in the fat. Particularly in the neighborhood of the pancreas, where they are most numerous, foci of necrosis may be large and confluent, giving a tallow-like whiteness to extensive areas of fat. Discrete foci in greater or less number may stud the perinephritic fat, the mesocolon, the mesentery, and the omentum. Foci of necrosis occur less frequently below the parietal peritoneum and upon the surface of the diaphragm.

In some instances fat necrosis has extended beyond the peritoneal cavity. Hansemann has twice seen foci of necrosis in the subcutaneous fat, while in several instances the fat of the pericardial and pleural cavities has been implicated. Chiari has described a remarkable instance of widespread fat necrosis. Gangrenous pancreatitis had caused such complete disintegration of the gland that the duct of Wirsung was eroded and communicated directly with the cavity of the bursa omentalis; areas of the fat necrosis, often the size of a pea, were present about the lesser peritoneal cavity, in the mesentery, in the subperitoneal fat of the abdominal wall, in the subpericardial and subpleural fat, and in the subcutaneous tissue.

Microscopic examination of the foci of necrosis shows that the cells, of which the outlines are still preserved, although the nuclei have disappeared, contain at an early stage crystals of fatty acid. Calcium

<sup>1</sup> *Berliner klin. Woch.*, 1902, xxxix, 734.



salts combine with these fatty acids to form calcium salts readily demonstrable by microchemical reactions. A few polynuclear leukocytes find their way into the necrotic tissue, but when numerous their presence is due to secondary infection. According to Wells the lesion experimentally produced may be recognizable three hours after the application of pancreatin to fat. Proliferation of fixed tissue cells occurs in the periphery of the necrotic area. The lesion may so completely disappear that its site is no longer recognizable. Wells found fat necrosis in a dog of which the abdomen was opened four days after the injection of pancreatin, but seven days later the lesion had completely disappeared. In a case of acute cholecystitis Körte found at operation typical areas of fat necrosis; the patient recovered, but at a second operation, undertaken a year later for the relief of symptoms suggesting the presence of a gallstone in the common bile duct, foci of necrosis were no longer present.

**Clinical Significance of Fat Necrosis.**—The facts already cited demonstrate that the lesion is caused by pancreatic juice diverted from its proper channels into the tissues about the gland. When the outflow of bile is obstructed, the bile dammed back upon the liver reaches the interstitial tissue of the gland, and hence is transported to all parts of the body. When the secretion of the pancreas, likewise dammed back upon the gland, reaches the interstitial tissue of the organ, and hence, probably by way of the tissue spaces finds its way into tissues at some distance from the gland, its presence is not indicated by any colored constituent; as yet, moreover, there is no certain means of identifying constituents of the pancreatic juice in the urine. Focal fat necrosis is in such case the only readily recognizable effect of the aberrant secretion, and for diagnosis of pancreatic disease is available only to the surgeon who opens the abdomen. Hansemann has mentioned a unique case in which circumscribed areas of cutaneous injections marked the site of foci of necrosis shown by postmortem examination to be situated in the subcutaneous tissue of the abdominal wall, but rarely does the characteristic lesion implicate fat outside of the abdominal cavity.

Since disseminated foci of fat necrosis indicate in most instances acute hemorrhagic or gangrenous pancreatitis, its recognition at operation is of great importance. By those who have not previously seen the lesion it may be mistaken for caseous miliary tubercles or for carcinomatous nodules which have undergone necrosis, but the absence of elevation or other evidence of newly formed tissue shows that necrosis has affected the fat.

Since abundant evidence has shown that fat necrosis is due to the action of the fat-splitting ferment secreted by the pancreas, the possibility suggests itself that the ferment which is free in the tissues may be excreted by the kidneys. Recognition in the urine of a fat-splitting ferment derived from the pancreas would afford means for the diagnosis of obscure pancreatic disease accompanied by fat necrosis. With the urine removed at autopsy from the bladder of an individual dead with acute hemorrhagic pancreatitis and fat necrosis, the writer obtained a reaction which indicated the presence of the fat-splitting ferment. The method of identifying this enzyme was that described by Kastle and Loevenhart,

who showed that the presence of fat-splitting ferment may be demonstrated by use of ethyl butyrate. Experiments of Hewlett<sup>1</sup> show that a variety of injuries to the pancreas of dogs is followed by the appearance in the urine of a ferment which is capable of decomposing ethyl butyrate into butyric acid and alcohol. Very little if any of such ferment is present in the normal urine; after obstruction of the pancreatic duct he found it during a period of from three to five days, but it is present in greatest amount as the result of experimental hemorrhagic pancreatitis. The method which Hewlett describes in detail can be used to examine the urine when pancreatic disease with fat necrosis is suspected.

### HEMORRHAGIC NECROSIS OF THE PANCREAS

The Middleton-Goldsmith Lecture of Fitz, published in 1889, contains a classification of acute pancreatic diseases which served as a basis for the first accurate description of their symptomatology. He found that acute inflammation of the gland may be hemorrhagic, gangrenous, or suppurative. His description of the symptomatology of so-called acute hemorrhagic pancreatitis has made typical instances of the condition recognizable during life. Gangrenous pancreatitis, according to Fitz, although it may follow other conditions, is usually the result of the hemorrhagic lesion. Suppurative pancreatitis resembles suppurative inflammation of other organs. Fitz noted the relationship of so-called fat necroses to acute pancreatic disease, already suggested by Chiari, and found that it more frequently accompanied hemorrhagic and gangrenous than suppurative inflammation.

Suppurative pancreatitis does not differ from similar lesions of other organs and is described in a special section (page 622). Study of the changes which occur with the hemorrhagic and gangrenous lesions of the gland shows that necrosis is the underlying change. Inflammation is absent at the onset of the disease. Experimental studies have shown that the lesion with all the characters which occur in man, can be reproduced in animals by a variety of irritants which produce necrosis of the pancreatic parenchyma. Necrosis implicating the walls of bloodvessels is accompanied by hemorrhage and at the margin of the necrotic tissue there is accumulation of inflammatory products. The condition described as gangrene, characterized by discoloration and softening of necrotic tissue infiltrated with blood, represents a late stage of the same lesion. It is unnecessary to describe gangrenous pancreatitis as a disease separable from hemorrhagic necrosis.

**Pancreatic Hemorrhage.**—Those who have systematically described diseases of the pancreas have given special consideration to so-called *pancreatic apoplexy* or hemorrhage into the pancreas; the condition has medicolegal interest, since it is believed to be one of the causes of sudden death. Hemorrhage into the substance of the gland may be caused by traumatism, or by malignant growth, and minute extravasations

<sup>1</sup> *Jour. Med. Research*, 1904, xi, 377.

may be associated with various infectious diseases; such hemorrhage presents nothing peculiar to the organ. The literature contains numerous cases in which a hemorrhagic lesion of the gland has been the only explanation of the rapidly fatal illness of an apparently healthy individual. In some cases cited as examples of pancreatic hemorrhage, as Seitz explains, it is improbable that the pancreatic lesion has been the cause; whereas, in other cases, such as those described by Reubold and Rehm, after poisoning with morphine, after strangling, or after hemorrhage from the femoral vein, the amount of blood in and about the gland has been so small that it may be referred to the hemorrhagic extravasation which Chiari has described in association with postmortem or agonal self-digestion.

Numerous cases have demonstrated that extensive hemorrhage into the peripancreatic tissues may occur with so-called hemorrhagic pancreatitis; necrosis is primary, and the hemorrhage and inflammation are its consequences. When both inflammation and hemorrhage coexist, the difficulty of deciding which preceded the other is obviously great, for an accumulation of blood in and about the duodenum would quickly become the seat of bacterial infection, and an abscess cavity would be formed. The existence of hemorrhage without evidence of inflammation has been believed to demonstrate the occurrence of so-called apoplexy. Atheroma of arteries and fatty degeneration of the pancreatic parenchyma, cited as causes of hemorrhage, have been found in only a limited number of cases. Knowledge of the pathology of hemorrhagic necrosis of the pancreas, recently acquired, has facilitated the description of such cases, and the literature of the last few years contains few, if any, instances of so-called apoplexy. An instance of pancreatic hemorrhage is described by Simpson. The pancreas was the seat of hemorrhagic infiltration and the organ was surrounded by semifluid clotted blood. In view of subsequent observations the presence of a gall-stone lodged at the orifice of the common bile duct leaves little doubt that this case is a typical example of hemorrhagic necrosis. It is improbable that the pancreas is more susceptible to hemorrhage than other parenchymatous organs.

**Etiology.**—Hemorrhagic necrosis of the pancreas occurs more frequently in men than in women. Among 41 instances of the hemorrhagic lesion Körte found 37 were in males and 4 in females; in 40 cases of so-called gangrenous pancreatitis, 21 were in males and 19 in females. The disease appears to have a more rapidly fatal course in men than in women. Of 121 cases of hemorrhagic and gangrenous pancreatitis cited by Peiser,<sup>1</sup> 79 were in males and 42 in females. The greater number of cases occur between the ages of twenty and fifty years.

A variety of conditions has been believed to favor the disease. Individuals in apparent good health are not infrequently attacked; those with abundant adipose tissue are said to be specially susceptible. About half the cases of hemorrhagic and of gangrenous pancreatitis, Fitz found, are preceded by attacks of indigestion, accompanied



by pain either referred to the region of the stomach or believed to be biliary colic. In a few instances anatomical evidence of *gastritis* and *duodenitis* has been obtained, but its etiological relation is doubtful. In two cases Simon and Stanley found intense gastroduodenitis with cellular infiltration of the duodenal submucosa, and since the duct of Wirsung was inflamed, they thought that the pancreatic lesion was the result of ascending inflammation. In one of these cases there was jaundice, and a calculus was found in the gall-bladder; the passage of a gall-stone may perhaps explain the occurrence of the lesion of the pancreas. In a case of Reynold and Moore there was gangrenous duodenitis, and in six cases cited by Gessner there was severe gastritis. It is not improbable that such lesions may be secondary to the pancreatic disease. It has been suggested by Peiser, who has described a case in which hemorrhagic pancreatitis occurred two and a half weeks after *childbirth*, that pregnancy may favor its onset. Of the 8 cases which he cites, 5 occurred from five weeks to five months after labor and the relationship is doubtful.

From the hemorrhagic pancreas and from the associated foci of fat necrosis, a variety of *bacteria*, in many instances *B. coli*, has been isolated, but according to almost all observers the results of bacteriological examination, which have been very inconstant, indicate that the various organisms bear no etiological relation to the disease and are secondary invaders. The acutely inflamed gland may contain no bacteria.

**Experimental Pancreatitis.**—Experiments of Hlava have shown that the lesion of acute hemorrhagic pancreatitis can be reproduced by injecting artificial gastric juice into the pancreatic ducts of dogs. A similar lesion which has followed the introduction of cultures of *B. coli*, *B. lactis aërogenes*, and *B. capsulatus* of Friedlander, the same writer has attributed to the acid products of these organisms. Carnot reproduced the lesion by injecting diphtheria toxin, and Flexner used weak solutions of hydrochloric, nitric, and chromic acids, sodium hydroxide, and formalin. Hlava has suggested that gastric juice may be driven by antiperistaltic action of the intestine into the pancreatic ducts. In a case described by Opie and Meakins<sup>1</sup> hemorrhagic necrosis was limited to the domain of an unusually large accessory pancreatic duct which entered the duodenum between the pylorus and the orifice of the common bile duct.

**Traumatic Pancreatitis.**—Hemorrhagic and gangrenous pancreatitis with disseminated fat necrosis has in a few instances so directly followed abdominal injury that the relation to traumatism cannot be doubted. Injury to the pancreas is usually associated with such severe damage to adjacent structures that a fatal result is rarely referable to the gland. Incisions into the pancreas of animals heal readily, while in 7 of 12 cases cited by Mikulicz-Radecki recovery occurred, although operation had demonstrated a wound of the pancreas. In a small number of cases hemorrhagic and gangrenous pancreatitis has followed blows upon the epigastric region which have not produced superficial wounds. A case is described by Selberg. A man, aged thirty-eight years, was kicked

<sup>1</sup> *Jour. Exp. Med.*, 1908.

by a horse in the region of the stomach, and was for a time unconscious. There was pain and tenderness in the epigastric region, with gradual distension and vomiting. The temperature remained normal. At autopsy there was generalized fibrinopurulent peritonitis. The omentum was studded with foci of fat necrosis; the head of the pancreas was wholly necrotic, and the remainder of the organ was infiltrated with blood.

Little is known concerning the pathogenesis of traumatic gangrene of the pancreas. Thrombosis of bloodvessels may perhaps explain the lesion. Repeating the experiments of Hildebrand and Dettmer and subsequent observers, Doberauer has shown that obstruction to the circulation, together with other injury to the gland, may be followed by hemorrhagic necrosis of the pancreas and fat necrosis.

**Cholelithiasis.**—Acute hemorrhagic pancreatitis is not infrequently associated with cholelithiasis. In 1903 it was possible to collect from the literature 37 cases in which hemorrhagic or gangrenous lesions were associated with gall-stones, and at least 9 similar cases have since been described. In 9 cases of the hemorrhagic lesion a calculus has been lodged near the termination of the bile duct, and one case examined by the writer<sup>1</sup> disclosed a mechanism by which a biliary calculus can produce the lesion. A corpulent man, aged forty-eight years, who had suffered with attacks of indigestion, was suddenly seized with severe pain in the abdomen, accompanied by nausea. The pain diminished in severity, but two days before his death returned with its former intensity. At autopsy widely disseminated fat necrosis was found, and the pancreas, which was much enlarged, had an almost uniform reddish-black color. A small gall-stone had lodged at the orifice of the diverticulum of Vater so that it had converted the common bile duct and the duct of Wirsung into a continuous closed channel, from which neither bile nor pancreatic juice could escape. Bile had penetrated into the pancreatic duct, doubtless injected by the gall-bladder. Bacteriological examination of the pancreas gave negative results. Experiments on dogs demonstrated that the bile of one animal injected into the pancreatic duct of a second is capable of causing typical hemorrhagic pancreatitis, which is fatal often within twenty-four hours. Bunting<sup>2</sup> has described a case almost identical with that just cited.

No data at present available indicate with how great frequency acute hemorrhagic pancreatitis is caused by gall-stones. In 5 of 8 cases seen by the writer cholelithiasis was present, and in 2 of these cases calculi were found lodged at the orifice of the common bile duct. In many cases gall-stones have been overlooked at autopsy. It is noteworthy that the gall-stones usually found in the bile passages and in the gall-bladder in these cases have been of such small size that they might readily occlude the duodenal orifice of the diverticulum of Vater without closing the communication between the common bile duct and the duct of Wirsung. In only a limited number of individuals is the anatomical structure of the diverticulum of Vater such that a calculus could convert the two ducts into a continuous closed channel. In 1 of 10 individuals the two

<sup>1</sup> *Johns Hopkins Hospital Bulletin*, 1901, xiv, 182.

<sup>2</sup> *Ibid.*, 1906, xvii, 265.

ducts have no common channel but open separately at the summit of the bile papilla, and in only 32 of 100 normal specimens which have been examined was the diverticulum of Vater of such size that a small calculus might occlude its orifice without completely filling it and thus obstructing one or both ducts which enter it.

**Special Pathology.**—The appearance of the pancreas varies with the duration of the disease. In instances in which death has occurred within forty-eight hours after the onset the organ is much enlarged, and in swelling assumes an irregularly cylindrical shape. The areolar tissue in the neighborhood of the gland may be infiltrated with blood and the lesser peritoneal cavity usually contains blood or blood-stained fluid. Opaque white foci of fat necrosis studding the retroperitoneal fat, transverse mesocolon, perhaps the mesentery elsewhere, and the subperitoneal tissue of the abdominal walls, are abundant, particularly in the immediate neighborhood of the gland. The tissue of the pancreas is firm in consistence and has in large part assumed a dark red, reddish-brown, or even reddish-black color, and not infrequently presents a mottled or marbled appearance due to the presence of sharply defined areas of yellowish white, relatively normal parenchyma. The proportion of transformed parenchyma varies considerably in different cases, but rarely, if ever, is the entire parenchyma affected by the lesion.

Characteristic of the lesion is the widespread necrosis which affects secreting parenchyma, interstitial tissue, and the walls of bloodvessels. Cells are transformed into homogenous structures without nuclei. The architecture of the tissue may be preserved, but outlines of acini and fibrous tissue are often completely lost. Transition from such areas of complete death of tissue to normal parenchyma is abrupt and marked by a zone containing fragments of nuclei, polynuclear leukocytes, red-blood corpuscles, and fibrin. The interstitial tissue of the parenchyma which is still intact is infiltrated with blood, while in the necrotic and partially disintegrated areas occur larger collections of much changed blood. Soon after the onset inflammatory products, particularly leukocytes and fibrin, are found at the margin of the relatively normal tissue.

The pathogenesis of the condition is best studied in the experimental lesion, which does not differ from that which occurs in human cases. Bile and a variety of irritant substances coming in contact with cells of the secreting parenchyma cause their death, and necrosis is associated with such injury to the walls of bloodvessels that red-blood corpuscles escape in great quantity. Hemorrhage may be the result of necrosis before inflammatory changes are well marked, but very quickly evidence of inflammation is found at the margin of relatively intact parenchyma. Flexner and Pearce have shown that degeneration, hemorrhage, and emigration of leukocytes occur within one or two hours after the injection of artificial gastric juice into the pancreatic duct of dogs. There is probably much truth in the suggestion of Klebs that hemorrhage is the result of corrosive action of the pancreatic juice. The various irritant substances which produce the lesion acting injuriously upon the tissue of the organ not improbably subject it to the action of its own secretion.



**Gangrene of the Pancreas.**—Fitz showed that acute hemorrhagic pancreatitis may terminate in the condition known as gangrene and in at least half of the recorded cases of what he designated gangrenous pancreatitis there was evidence of hemorrhage. In cases of hemorrhagic pancreatitis which have survived a week or more the gland assumes a dark red, reddish-black or black color, and the tissue is dry and covered by changed blood. At the end of the second week the organ may form a soft, black, friable mass, while the lesser omental cavity contains chocolate-colored fluid in which are bluish-black spots. Yellowish spots of softening may occur in the pancreas and the gland may be finally transformed into a soft mass attached by only a few shreds of tissue to the abdominal wall, or, having undergone complete sequestration, according to the description of some observers may lie free in the omental cavity. In such cases the lesser peritoneal cavity is distended with dark bloody or blackish, often foul-smelling, fluid containing particles of necrotic tissue. Infection with a variety of bacteria has occurred, and the abscess cavity thus formed is limited by the lesser peritoneal cavity; the foramen of Winslow is closed by adhesions, and there is in most instances no general peritonitis. The fat about the pancreas and in the wall of the lesser peritoneum is the seat of confluent areas of fat necrosis which as the result of softening and erosion show an irregular surface.

In some instances an extension of the abscess cavity forms a pocket in the retroperitoneal tissue over the left kidney. Perforations, usually with ragged frayed edges, may be found in the wall of the stomach or duodenum, doubtless caused by penetration of the abscess into the viscus. In a case described by Chiari there were two perforations into the stomach and five into the jejunum. In a case recorded by Chiari part of the gangrenous pancreas was passed from the rectum.

When, with the experimental lesion, recovery ensues, active proliferation of connective tissue occurs and the newly formed tissue invades and in part or wholly replaces the necrotic parenchyma. Evidences of such reparative changes have been found in patients who have survived the severity of onset, and is doubtless present in the comparatively small number of instances in which complete recovery occurs.

**Symptoms.**—Fitz carefully defined the symptoms of hemorrhagic and of gangrenous pancreatitis, and although he recognized that many cases showed varying combinations of the lesions thus designated, described them separately. Most writers who have subsequently described instances of either condition have adopted the classification of Fitz and have used that designation which more accurately describes the anatomical changes which have been found.

**Course.**—In those cases in which death occurs within a few days after the onset the hemorrhagic character of the lesion is predominant, and those cases which pursue a rapidly fatal course have been described as hemorrhagic pancreatitis. The relation between the duration of the disease and the character of the changes found after death varies considerably, but toward the end of the second week, and in many instances earlier, the pancreas has assumed the appearance described as gangrenous, and those cases have been described as gangrenous pancreatitis in which

either the initial symptoms of shock have not been fatal or the onset has been unusually mild. Since the disease apparently pursues a more violent course in men than in women, the hemorrhagic lesion has been more frequently encountered at autopsy in men. When the disease has assumed the subacute course which characterizes most cases of what has been called gangrenous pancreatitis, symptoms due to suppuration and accumulation of exudate in the lesser peritoneal cavity appear.

**Stage of Hemorrhagic Necrosis.**—Characteristic of the acute disease is its sudden onset, the severity of the pain which is localized in the epigastric region, and the associated symptoms of shock and intense depression of the circulatory system. One group of cases described by Nimier as *foudroyant* terminate fatally within a few hours. Such cases have been described as instances of pancreatic hemorrhage or apoplexy. In a large proportion of instances death occurs within the first four or five days, while about half of the cases pursue a subacute course, death occurring after several weeks or months.

The disease in many instances affects individuals who have suffered with repeated attacks of abdominal pain, but in many cases the patients have had good health, robust men often somewhat corpulent being not infrequently affected. *The preceding attacks of pain* are of two kinds, being referable either to the gastro-intestinal tract or to the bile passages. In nearly one-half of the cases collected by Fitz there had been attacks of indigestion, with pain at times of great severity, nausea, and vomiting. He regarded the previous digestive disturbance as gastric or gastroduodenal rather than enteric. In about one-fifth of the recorded cases, according to Gessner,<sup>1</sup> there have been, perhaps for several years, typical attacks of gall-stone colic often accompanied by jaundice, until an attack of unusual severity is accompanied by symptoms of collapse.

*The pain of onset*, which appears with surprising suddenness, is of great violence and is localized above the umbilicus; it may be constant or occur in paroxysms, and in the acutely fatal cases persists until death. The pain has been occasionally described as present above the umbilicus and to the left of the median line following the course of the pancreas, but the seat of greatest intensity may be the left or right hypochondrium, or even the lower abdominal region. The epigastric region is sensitive to pressure, and there is usually rigidity of the abdominal muscles. Intense pain in the back radiating toward the legs has been described.

The appearance of pain is rapidly followed by *vomiting*, rarely by nausea alone. Vomiting may recur at short intervals or may stop for several hours or even several days, to be repeated with perhaps equal severity. The vomitus is usually copious and bile-stained, but may be mucous, and in several instances has been dark brown or bloody.

*Symptoms of shock* accompany the pain and vomiting of onset and usually precede death. There is profound weakness; the pulse is accelerated, and in several instances cyanosis has been a conspicuous symptom. Experiments of Gulecke, Doberauer, and Egdahl<sup>2</sup> indicate that substances

<sup>1</sup> *Deutsche Zeit. f. Chir.*, 1899, xlv, 65.

<sup>2</sup> *Journal of Experimental Medicine*, 1907, ix, 385.

perhaps formed by autodigestion of pancreatic tissue depress the circulation and cause profound poisoning.

Although the abdomen is rigid and often distended, particularly in the epigastric region, a *tumor mass* referable to the pancreas is rarely if ever palpable.

In about one-half of the cases there is *constipation*, but in a considerable number of cases *diarrhœa* is present from the beginning or may follow constipation. The occurrence of constipation in association with the severe symptoms of onset has made the diagnosis of intestinal obstruction in such cases frequent, and the nature of the disease has been determined at operation undertaken with the purpose of relieving obstruction. Gessner states that passage of feces occurs spontaneously or as the result of enemata in many cases on the fourth day. In six cases collected by this author the enlarged head of the pancreas was found either at autopsy or at operation to encroach upon the lumen of the duodenum, but in most cases no anatomical evidence of obstruction has explained the symptoms of intestinal obstruction. It has been suggested that irritation of the solar plexus by hemorrhage or by pressure may favor the occurrence of constipation. The stools are not infrequently clay-colored; in only one case (Chantemesse and Griffon) fatty stools were present, although death occurred two days after the onset of symptoms. The feces rarely contain blood.

*Jaundice*, varying in intensity, was present in 10 per cent. of the cases collected by Gessner, who has given special attention to the relation between acute pancreatitis and disease of the biliary passages. *Fever* is rarely present during the early stage and with symptoms of collapse the temperature may be subnormal. Elevation of temperature with chill has been observed. *Leukocytosis* has been found in cases in which the blood has been examined. In a case of Hunt<sup>1</sup> the leukocytes numbered 37,000 per cmm. on the first day of the disease. In a case of Sendler their number was not increased. *Diastase* in the feces and urine may be measured by a method introduced by Wohlgemuth; Wynhausen<sup>2</sup> found the enzyme in the feces greatly diminished in two cases of hemorrhagic pancreatitis. Wohlgemuth found that experimental occlusion of the pancreatic ducts caused well-marked increase of diastase in the urine, and Hirschberg<sup>3</sup> was able to demonstrate a similar increase in two cases of so-called acute pancreatitis. *Glycosuria* has occurred in only a small proportion of cases of hemorrhagic pancreatitis (Benda and Stadelmann, Cutler, Sarfert and Simmonds). The case of Benda and Stadelmann is noteworthy, because the symptoms were those of rapidly fatal diabetic coma. The patient became comatose soon after the onset of violent abdominal pain; 3.4 per cent. of sugar was found in the urine. The pancreas, with the exception of a part of the head, formed a soft, bloody mass.

**Stage of Gangrene.**—Cases in which the early stage has been survived have been described as instances of gangrenous pancreatitis. At the

<sup>1</sup> *Boston Medical and Surgical Journal*, 1905.

<sup>2</sup> *Berliner klin. Woch.*, 1909, xlii, 1406.

<sup>3</sup> *München. med. Woch.*, 1908, lv, 225.



end of several days—Gessner regards the fourth day as critical—the symptoms of onset may diminish in violence; pain and tenderness in the epigastric region are still present, or may recur at intervals, and are not infrequently associated with vomiting. Constipation, if present, disappears and may be followed by diarrhoea. Symptoms which indicate the presence of so-called gangrene, with bacterial invasion of the necrotic gland and adjacent peritoneal surfaces, are fever and epigastric tumor. The transition to the stage of necrosis and suppuration usually occurs toward the end of the second week.

The *temperature*, which during the early stage shows no elevation, is moderately increased and irregular. Although usually little more than 100°, it may reach 104° F., and in some instances there are repeated chills. The disease may, however, pursue its course without fever. *Leukocytosis* was present in two cases of gangrenous pancreatitis described by Thayer. In one case the leukocytes on the nineteenth day numbered 18,300; in the second case during the fourth week they numbered 33,700, although the temperature at the same time varied from 97.6° to 98.6° F.

The *tumor mass*, due in great part at least to accumulation of exudate in the lesser peritoneal cavity, usually appears in the epigastric region and, extending toward the spleen, varies considerably in size and distinctness. It has been described at times as a rounded mass the size of a child's head situated above the umbilicus, while in other cases there has been an ill-defined resistance in the same region. In all of 5 cases of gangrenous pancreatitis Körte found a tumor mass which in 3 instances was first found on the left side in the region of the left hypochondrium and flank, subsequently becoming palpable between stomach and colon. In 5 cases described by Thayer a tumor mass was found in the epigastric region; in 2 cases pancreatic gangrene was demonstrated by autopsy, while in 3 recovery followed operation and the nature of the lesion was not clearly defined.

In stout individuals palpation may be difficult, but is facilitated by the emaciation which usually occurs with long continuance of the disease. The muscular spasm which hinders palpation during the acute stage disappears. The lower border of the tumor mass may descend with respiration; occasionally pulsation is transmitted from the aorta, and has been found to disappear in the knee-chest position. Inflation of the stomach and perhaps of the colon may aid in the localization of the mass. Tympany of the stomach separates the mass from the liver, and after inflation of the viscus tends to cover it. The colon lies along the lower border of a tumor mass due to an exudate within the lesser peritoneal cavity. When the abscess cavity eroding the tissue over the left kidney tends to make its way toward the left lumbar region, resistance may be felt below the left costal margin extending downward as far as the rim of the pelvis.

The stools, which are not infrequently diarrhoeal, in a few instances have contained blood. Steatorrhoea has rarely if ever been observed, but in a case of von Noorden's chemical examination showed that the proportion of split fat in the feces was greatly diminished. In 2 cases

described by Chiari recovery followed the expulsion from the rectum of necrotic pancreatic tissue.

*Jaundice* may occur, and was present in one-fifth of the cases of gangrenous pancreatitis collected by Fitz.

*Glycosuria* is an infrequent symptom of pancreatic necrosis. In the cases of Israel and of Fleiner the disease occurred in individuals who had previously suffered from diabetes. In the case of Middleton sugar was found in the urine removed from the bladder at autopsy. In the case of Brentano 6 per cent. of sugar was found in the urine ten days after operation and four days after the discharge from the wound of a mass of necrotic tissue 12 cm. in length; previous examination of the urine had not been made. Peiser found sugar in the urine two months after the onset of symptoms; it is probable that almost the entire gland was affected, since a few days after the operation a sequestrum of pancreatic tissue 19 cm. in length was discharged from the wound.

**Complications and Sequelæ.**—The most important complications—namely, cholelithiasis and suppurative peritonitis affecting the lesser peritoneal cavity—have been described. Erosion of the tissue over the left kidney and sinking of the bursal abscess toward the left lumbar region has also been mentioned. Perforation of the stomach, duodenum, and transverse colon occur not infrequently, and in a case described by Thayer the three organs were the seat of erosion. Blood or fetid pus rarely appears in the feces as the result of such accidents. Within the necrotic tissue of the pancreas bloodvessels become the seat of thrombi which not infrequently extend to adjacent vascular trunks. The splenic vein may be occluded and in a case described by Fitz thrombosis of the splenic vein was present in a patient who died ten days after the onset.

Diabetes is infrequently associated with pancreatic gangrene, but may occur either as a complication or a sequel. Such instances have already been cited. In a case of Körte 2 per cent. of sugar was found in the urine twenty months after an operation at which necrotic pancreatic tissue had been removed. Sugar was not present before or immediately after operation; seven years after operation the patient was living but much emaciated as the result of diabetes.

An unusual accident has been described by Langdon. Two years after an operation, at which bloody fluid had been removed from the lesser peritoneal cavity, death occurred suddenly. The pancreas was in large part replaced by scar tissue; the scar was in contact with the portal vein from which fatal hemorrhage had occurred.

In a considerable number of cases pancreatic and peripancreatic *cysts* are preceded by acute symptoms which are similar to those of hemorrhagic pancreatitis, but in most instances it is impossible to determine by anatomical examination after a considerable lapse of time the character of the primary pancreatic lesion. A few cases indicate that peripancreatic cysts formed within the bursa omentalis or even pancreatic cysts may follow hemorrhagic pancreatitis. In a case described by Francke<sup>1</sup> intense pain associated with vomiting appeared with great suddenness;

<sup>1</sup> *Deutsch. Zeit. f. Chir.*, 1900, liv, 399.

two weeks later a tumor was found in the left hypochondriac region and gradually increased in size. At operation, five weeks after onset, an elastic thin-walled cyst, the size of a man's head, occupied the lesser peritoneum and surrounded the pancreas, which was the seat of necrosis and old hemorrhage; foci of fat necrosis were present in the omentum and mesentery. In a similar case of Rasumosky a tumor mass in the epigastrium was noted five hours after the onset of symptoms, and at operation three weeks later was found to be due to a cyst in which necrotic pancreatic tissue was found. Adler<sup>1</sup> has described a so-called pseudocyst of the pancreas which was probably the result of acute hemorrhagic pancreatitis; the pancreas which formed part of the cyst wall was necrotic and the site of old hemorrhage. When blood and necrotic pancreatic tissue remain sterile the digestive ferments of the pancreas may perhaps cause softening and encapsulation by fibrous tissue. The possibility that this process might take place wholly within the substance of the pancreas is suggested by a case of acute hemorrhagic pancreatitis with fat necrosis described by Dressel; a cavity filled with clotted blood the size of a child's head was present within the substance of the gland.

**Diagnosis.**—For the recognition of hemorrhagic necrosis of the pancreas the mode of onset is important—namely, its suddenness and violence with intense epigastric pain, vomiting, and symptoms of profound collapse. When hemorrhagic necrosis accompanied by constipation resembles intestinal obstruction, the epigastric localization of pain and distension, the intensity of the pain, and collapse point to pancreatic disease. Stercoraceous vomiting is rarely present, and the increase of peristalsis recognizable with intestinal obstruction is not present.

Since the disease may be preceded by repeated attacks of typical biliary colic, and when caused by the lodgement of a small calculus in the diverticulum of Vater is associated with symptoms of gall-stones, a differential diagnosis may be very difficult. When an *attack of biliary colic* is accompanied by pain of unusual intensity, present throughout the epigastric region and perhaps more intense on the left side, especially when there are symptoms of sudden and profound collapse, hemorrhagic pancreatitis should be suspected. With *perforation of the gall-bladder* following cholecystitis the symptoms are usually localized on the right side. Ulcerative processes associated perhaps with malignant tumors of the stomach, duodenum, or transverse colon may produce *suppurative inflammation limited to the lesser peritoneal cavity*, particularly when they cause perforation. The suddenness of onset, the intensity of the pain, and the rapidity of collapse indicate the presence of hemorrhagic necrosis of the pancreas, especially when there is no history suggesting gastric or duodenal ulcer or other lesion which might cause perforation of the stomach, duodenum, or transverse colon. Pulsation of a tumor caused by exudate in the lesser peritoneal cavity, being transmitted from the aorta, is not expansile and disappears when the patient rests upon his side or on knees and elbows; Langdon has described such a case simulating *ruptured aneurism*.

<sup>1</sup> *Virchows Archiv*, 1904, clxxvii, Suppl. Heft 154.



When the disease has assumed a subacute course, the recognition of a tumor mass in the epigastric region between stomach and colon suggests the presence of an exudate within the bursa omentalis, but gives positive evidence of pancreatic gangrene only when its appearance follows the acute symptoms already described. Symptoms indicating disturbed pancreatic function such as glycosuria or steatorrhœa are rarely present, but both in the acute and subacute stages chemical methods applied to the examination of urine and feces may give additional information.

**Treatment.**—Although pancreatic necrosis cannot be directly influenced by any available means, in some instances the profound collapse of onset may be overcome, so that the disease may reach the subacute stage, in which it is more susceptible to successful surgical interference. Intense epigastric pain usually requires morphine, but in several instances the violent pains of onset have been controllable only by inhalation of chloroform. For the vomiting Körte recommends the withholding of food and lavage of the stomach. Enemata of warm water may serve to overcome constipation and distension, while stimulating and nutrient enemata may serve to sustain the strength. For collapse subcutaneous or intravenous infusions of normal salt solution may be employed.

The value of operation during the early stage, when symptoms of circulatory depression are predominant, has been much disputed. Loss of blood is rarely an important feature and it is improbable that hemorrhage from the necrotic tissue could be controlled under the condition which such an operation would present. A mistaken diagnosis, usually of intestinal obstruction, has been the incentive for a majority of the operations undertaken at this stage, and the recognition of characteristic foci of disseminated fat necrosis in the great omentum has given the first indication that the pancreas has been diseased. Careful searching of the intestine drawn out through the abdominal wound, together with prolonged anesthesia, has doubtless had an unfavorable result in many instances. Mikulicz-Radecki recommends evacuation of the hemorrhagic exudate contained in the lesser peritoneal cavity and free drainage of the omental bursa with gauze after exposure of the vault of the diaphragm by resection of the tenth and eleventh ribs, if necessary.

Statistics collected by Gessner indicate that operations undertaken up to the end of the second week and therefore during the stage of hemorrhagic inflammation, are much more frequently fatal than those undertaken at a later period when the disease has become subacute and so-called gangrene with peripancreatic abscess is present. Of 41 instances in which operation was performed upon patients suffering with the disease, 21 occurred during the first two weeks, and in only one case (Halsted) did recovery follow. In most instances a laparotomy in the middle line was performed, the nature of the disease was not determined, the abdomen was closed, and death followed within a few hours. Of 20 cases operated upon at a later period, when peripancreatic abscess had formed, 6 recovered. In the larger statistics of Mikulicz-Radecki, published about five years later (1903), there were 46 operations in the acute stage, with 9 recoveries, and 35 operations in the subacute stage, with 18 recoveries. This surgeon was unwilling to attribute much

significance to these figures, since the relative proportion of untreated cases which die in the first stage is unknown. He maintained that early operation limits the extent of necrosis and sequestrum formation, and gives diminished opportunity for serious complications, such as venous thrombosis and pyemia. Operation under local anesthesia may diminish the tendency to shock.

Since the disease is frequently caused by gall-stones, it is desirable to examine the biliary passages at operation, and to determine if calculi are present. The continued presence of a calculus at the duodenal orifice of the diverticulum of Vater may increase the severity of an existing lesion, and its removal is desirable. The calculus which causes the obstruction is usually of small size and not infrequently the gall-bladder has contained a large number of minute calculi, which during expulsion can perhaps repeatedly divert bile into the pancreatic duct. In a patient operated upon ten days after the onset of symptoms Kelly found fat necrosis; he removed from the gall-bladder about fifty very small calculi of almost uniform size; the patient recovered. That the existence of diabetes mellitus should not necessarily prevent operation for pancreatic necrosis is indicated by a case described by Peiser. Before operation the urine contained 4 per cent. of sugar, acetone, and diacetic acid; the excretion of sugar was not influenced by the evacuation of a peripancreatic abscess, accomplished by two operations. The patient lived five months after operation, and death was the result of diabetes mellitus.

### SUPPURATIVE PANCREATITIS

Suppurative inflammation of the pancreas, characterized by accumulation of inflammatory products and softening of tissue, with consequent formation of one or more cavities containing purulent fluid, does not differ from similar changes in other organs. In many instances the disease, which is the result of bacterial invasion, occurs as a primary infection, but in other cases it follows hemorrhagic necrosis of the pancreas, the hemorrhagic and necrotic tissue being particularly susceptible to bacterial infection; hence the so-called gangrenous pancreas may contain abscess cavities, and in such instances a distinction between gangrene and suppuration is impossible. Moreover, acute inflammation of the pancreas, which has persisted for several weeks, almost constantly extends to the lesser peritoneal cavity, which with bacterial invasion becomes the seat of suppurative inflammation. In many cases described as instances of suppurative pancreatitis operation has disclosed an abscess in this region, but no subsequent postmortem examination has shown the exact anatomical condition; in reports of many such cases no attempt has been made to distinguish between pancreatic and peripancreatic abscess. With gangrenous pancreatic inflammation, symptoms of peripancreatic abscess may be more conspicuous than those referable to the gland itself, and the lesion at autopsy, several weeks after the onset, may present nothing characteristic of the hemorrhagic and gangrenous lesion.

**Etiology.**—When suppurative inflammation is not the result of simple extension from an adjacent organ, there are two possible paths of infection—namely, the bloodvessels and the ducts. Metastatic abscesses are rarely found in the pancreas. Infection by the bloodvessels may explain some cases but more readily demonstrable and probably of far greater frequency is ascending infection by way of the ducts. Experimental studies show that suppurative lesions may follow the injection of bacteria into the pancreatic ducts. Suppurative pancreatitis has been produced by Körte and by Carrot by injection of bacilli of the colon group into the duct.

Valve-like folds within the diverticulum of Vater prevent the entrance of the duodenal contents, so that after death it is impossible to force material from the intestine into the duct. The flow of secretion doubtless exerts a protective influence by washing foreign material from the duct. Obstruction of the duct of Wirsung favors the entrance of microorganisms, and many cases of pancreatic suppuration are associated with occlusion of the duct of Wirsung by gall-stones lodged in the diverticulum of Vater, by pancreatic calculi, and by malignant growths compressing the duct. In a case described by Pearce multiple abscesses in the head of the pancreas followed obstruction of the duct by carcinoma of the diverticulum of Vater.

The probability of infection is much increased when the presence of gall-stones has previously caused suppurative inflammation of the bile ducts. In two cases of Mayo Robson's, abscess of the pancreas accompanied cholelithiasis with suppurative cholangitis. In a case of suppurative pancreatitis recorded by Dieckhoff biliary calculi had actually found their way into the duct of Wirsung. In a case described by Fuchs<sup>1</sup> it is probable that pancreatic abscess had been secondary to localized hemorrhagic necrosis caused by a gall-stone lodged in the diverticulum of Vater.

In the small number of cases in which bacteriological examination of the purulent fluid has been made, a variety of microorganisms has been found. In the case of Maas and of Etienne both cocci and bacilli were found. In one of the cases described by Fitz several varieties of bacilli and a staphylococcus were isolated. An organism resembling *Bacillus proteus* has been isolated (Hauser); Dieckhoff found diplococci resembling *Diplococcus pneumoniae* and in a case of Körte streptococci were found.

**Pathology.**—With acute inflammation of the pancreas there may be polynuclear leukocytes within and about the ducts of the gland, and the interstitial tissue may be distended by oedema. Such inflammation, which doubtless begins as an ascending infection of the ducts, does not necessarily proceed to suppuration, and may be unaccompanied by macroscopic change. It is, however, not improbable that similar infection of greater severity may cause diffuse suppuration in the organ.

In a case described by Etienne<sup>2</sup> the entire gland, which was enlarged, was infiltrated with thick, yellowish, purulent fluid, which collected upon the cut surface; drops of pus escaped from the incised ducts. In

<sup>1</sup> *Deutsch. med. Woch.*, 1902, xxviii, 829.

<sup>2</sup> *Arch. de méd. expér.*, 1898, x, 177.



other instances destruction of tissue is more advanced and the organ contains communicating cavities of irregular shape filled with pus, or there may be numerous isolated abscesses. In some cases almost total destruction of tissue has been described, a large cavity filled with pus being found to occupy the site of the pancreas. Localized abscesses may be situated in any part of the gland, but are most frequent in the head. The abscess cavity may be surrounded by a fibrous capsule. Fitz observed that fat necrosis occurs less frequently in association with suppurative inflammation than with hemorrhagic or gangrenous pancreatitis; foci of fat necrosis are found when purulent inflammation is the result of hemorrhagic pancreatitis.

**Symptoms.**—Since suppurative pancreatitis may occur as a complication of acute hemorrhagic pancreatitis, of lithiasis, of cyst, or of cancer, while it is sometimes the result of ascending infection from the inflamed duodenum or bile passages, its mode of onset and symptomatology vary considerably. In one group, including more than one-half of the cases collected by Körte, the onset is sudden and associated with intense epigastric pain, vomiting, and collapse; the symptoms of onset do not differ from those of hemorrhagic necrosis of the pancreas, and it is not improbable that in a considerable proportion of these cases infection and suppurative inflammation have followed hemorrhagic necrosis. The severity of the symptoms diminishes, and the disease in most instances pursues a chronic course, with exacerbations of pain and gastro-intestinal disturbance occurring at irregular intervals. In a smaller group the onset is gradual, and for a considerable time there is abdominal pain, or perhaps only a sense of discomfort in the epigastric region, together with gastric symptoms of variable intensity.

The tendency of suppurative pancreatitis to pursue a chronic course is shown by 14 cases cited by Fitz; 6 were fatal in the first month, 3 during the second month, and 5 between the fourth and eleventh months. In 22 of 46 cases collected by Körte death occurred between one month and one year after the onset. In a few cases death occurs more rapidly.

In most cases there is either *diarrhœa* or *constipation*, the former being present in considerably more than half of the cases. In the case described by Nicholas hemorrhage from the bowel occurred several times, and at autopsy an abscess in the pancreas was found to communicate by a fistulous opening with the duodenum. Hiccough was present in 5 cases collected by Etienne, in 2 of which it was incessant. In 2 of the cases peritonitis may have caused the symptoms. *Jaundice* occurs in a considerable number of cases, and may be due to cholelithiasis, which has afforded conditions favoring infection of the pancreatic ducts. Jaundice may be caused by an abscess situated in the head of the gland and compressing the bile ducts.

Symptoms indicating the occurrence of *suppuration* are fever and abdominal tumor. In the greater number of cases there is elevation of temperature, which is moderate in degree, but in some instances the temperature has been normal or even subnormal. In one group of cases, according to Fitz, the onset is violent and there are frequent chills and irregular, often high, temperature, exceeding 105° F.; chills may occur

at the onset and recur during the course of the disease. In another group of cases the early symptoms present little that suggests the presence of suppuration; there is loss of appetite, progressive weakness and emaciation, perhaps diarrhœa or jaundice, but no pain or fever. *Leukocytosis* has been present in cases in which purulent fluid has been removed from the lesser peritoneal cavity (Thayer, Murray).

A more or less clearly definable *tumor* mass occupying the position of the pancreas has been noted in hardly more than a fourth of the recorded cases (Körte), but when present this symptom is significant for both diagnosis and operative treatment. In many cases there is abdominal distension not infrequently localized in the epigastric region, and pain and tenderness in the same situation may further prevent satisfactory palpation, which may be more readily performed after the subsidence of the violent symptoms of onset. The detection of deep-seated resistance behind the stomach or between stomach and colon, absent perhaps during the early stage may suggest that the pancreas is the seat of disease.

Disturbances of *pancreatic function*, although significant when present, are not commonly associated with pancreatic abscess, which in most instances leaves relatively normal a considerable part of the gland. Glycosuria has been present in a small number of cases. *Emaciation* associated with suppurative pancreatitis is referred by some writers to functional disturbance of the gland, but is, in part at least, referable to continued suppuration. The accompanying weakness is often extreme.

**Sequelæ.**—*Peritonitis* due to extension of the inflammatory process to the surface of the organ and subsequent infection of adjacent serous surfaces is almost constantly associated with suppurative pancreatitis. Adhesions binding the posterior wall of the stomach to the pancreas may be the site of fistulous communications with this organ. Encysted peritonitis with effusion limited to the lesser peritoneal cavity is present in cases which pursue a subacute course. General peritonitis has been present in a considerable number of cases examined at autopsy. Rupture of the pancreatic or peripancreatic abscess may occur into a variety of organs. Perforation of the stomach or of the duodenum is not infrequent. Vomiting of purulent fluid and hemorrhage from the bowel have occasionally been associated with perforation of the duodenum. Rupture of an abscess into the general peritoneal cavity has been observed in 4 cases cited by Körte. Thrombosis of the splenic vein extending to the portal vein may occur. In a case described by Bamberger the portal and splenic veins were almost completely occluded by a thrombus which had undergone puriform softening in the neighborhood of an abscess in the head of the pancreas; the liver was enlarged and contained numerous abscesses, the largest of which was the size of a hen's egg. Abscesses in the left lobe of the liver were present in cases of Frison and of Drasche.

**Diagnosis.**—Since suppurative pancreatitis in a considerable number of instances follows hemorrhagic inflammation, the symptoms of onset are those of the last-named condition, and indeed, even at operation, the distinction between abscess of the pancreas and gangrenous inflammation with peripancreatic abscess is often difficult, although fortunately not of much clinical significance. It is not improbable, however, that

pancreatitis which is primarily suppurative may begin with equal severity. In another group of cases the onset is gradual, and there are vague symptoms of gastro-intestinal disturbance with epigastric pain of variable intensity; irregular fever, perhaps with chills, may suggest suppuration. When a deep-seated mass in the region of the pancreas appears, the diagnosis of peripancreatic abscess can be made, but it is rarely if ever possible to decide if peripancreatic abscess accompanies gangrenous inflammation or is the result of an abscess within the substance of the gland. Hence the differential diagnosis between hemorrhagic necrosis and suppurative pancreatitis is rarely possible, since, especially in the early stages the symptoms are those of hemorrhagic necrosis of the pancreas, although the early onset of fever with chills and irregular temperature may suggest primarily suppurative pancreatitis. The symptoms appearing in association with recognizable cyst, lithiasis, or neoplasm of the pancreas, may suggest that suppuration has occurred as a complication of one of these lesions.

When a tumor-like resistance can be felt in the epigastrium behind the stomach and colon, its ill-defined character and its rapid appearance in association with acute symptoms serve to distinguish it from cyst or carcinoma. Nevertheless, the difficulty of diagnosis, especially when the abscess is small, is well illustrated by a case cited by Thayer. An abscess at the junction of the head and body of the gland caused complete obstruction of the common bile duct and presented a picture suggesting carcinoma of the head of the pancreas or of the common bile duct.

**Treatment.**—Efficient treatment of abscess of the pancreas can be obtained only by surgical methods. Diagnosis is often impossible, but symptoms which indicate the occurrence of suppuration in or about the pancreas suggest the advisability of an exploratory laparotomy, and delay may be followed by grave complications, such as general peritonitis or thrombosis of the portal vein. Nevertheless, the success of surgical treatment is limited by the character of the lesion; with diffuse purulent infiltration and with multiple abscesses of the gland, surgical procedures, according to Körte, will probably be unsuccessful; but when a large accumulation of pus is present within or about the gland, incision of the abscess, removal of its contents, and drainage of the cavity offer opportunity for recovery. Suppuration within the substance of the gland is in most instances rapidly followed by peripancreatic suppuration, but the surgeon who has evacuated pus contained within the bursa omentalis may be unable to examine the gland with thoroughness. In some of the cases upon which operation has been performed an abscess cavity has been limited to the substance of the pancreas.

### CHRONIC INTERSTITIAL PANCREATITIS

Chronic inflammation is characterized by increase of interstitial tissue which partially replaces the parenchymatous cells, and is doubtless the most common disease to which the pancreas is subject. It is, however, accompanied by such ill-defined symptoms that it is rarely recognized



## PLATE XI

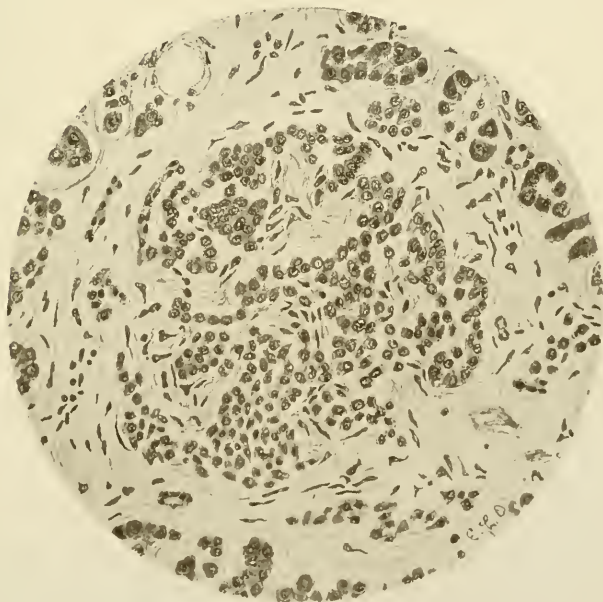
FIG. 1



Chronic Interstitial Pancreatitis Following Obstruction of Pancreatic Duct.

Showing unchanged islands of Langerhans embedded in sclerotic tissue.

FIG. 2



Chronic Interacinar Pancreatitis with Diabetes Mellitus.

Showing invasion of the islands of Langerhans by fibrous tissue.



during life unless an abdominal operation reveals its existence. When the lesion is associated with advanced destruction of the secreting parenchyma, digestive disturbances due to loss of pancreatic juice may result; in some cases the lesion is accompanied by diabetes mellitus.

**Etiology.**—The incidence is well illustrated by a series of 30 cases examined in the Johns Hopkins Hospital, 17 being in males and 13 in females. In five-sixths of the cases death occurred after the fortieth year, while more than two-thirds of the number occurred during the fifth and sixth decades of life. The relation of the disease to gall-stones, carcinoma, and cirrhosis of the liver explains its occurrence during and after middle life.

Partial and complete occlusion of the duct of Wirsung, brought about by pancreatic calculi within it, by large gall-stones lodged in the diverticulum of Vater, or by carcinoma or other new growth, is the most frequent cause. The two ducts of the pancreas anastomose within the gland in nine of ten individuals, and occasionally the duct of Santorini is of large size, being in one of ten cases as large or larger than the duct of Wirsung, but in a much greater number of subjects it is rudimentary in some part; the duodenal orifice especially is often very minute and cannot act as an outlet for the entire pancreatic secretion.

Ligation of the pancreatic ducts in animals is followed by chronic inflammation. The irritant action of the retained secretions and in many cases bacterial invasion of the obstructed duct combine to produce sclerosis, but in human cases the relative importance of the two factors is difficult to determine. Pancreatic calculi, for example, are doubtless in many instances at least produced by an infectious process within the ducts of the gland, and the associated sclerosis may be of such severity that the gland is converted into a fibrous band.

Much attention has been directed to the occurrence of chronic interstitial pancreatitis with cholelithiasis; the consequent induration of the gland when observed at operation undertaken for the removal of gall-stones has not infrequently been mistaken for carcinoma affecting the head of the pancreas. Riedel found in 3 of 122 operations upon the bile passages such dense induration of the head of the gland that malignant growth was suspected; 2 of these patients recovered, while autopsy in a third demonstrated the presence of chronic interstitial pancreatitis. Robson and Moynihan have described cases in which jaundice and other symptoms have suggested biliary colic, for the relief of which operation has been undertaken; the indurated condition of the head of the pancreas made a diagnosis of malignant disease not improbable, but the subsequent histories excluded this possibility. There is little doubt that chronic pancreatitis may follow cholelithiasis, even though no occlusion of the pancreatic duct has been caused by calculi; in such cases acute inflammation of the ducts of the pancreas accompanies similar inflammatory changes in the biliary passages consequent upon the presence of gall-stones in the gall-bladder. There is abundant evidence that ascending infection of the pancreatic duct, either from the inflamed bile passages or from the duodenum, may be a cause of chronic pancreatitis. Both Körte and Flexner have caused chronic pancreatitis by injecting colon bacilli



and other microorganisms into the pancreatic duct of animals. In cases of advanced chronic interstitial inflammation examined at autopsy, persistent vomiting accompanied by nausea and epigastric pain afforded evidence during life of gastric or gastro-intestinal disease. It is not improbable that the persistent vomiting produced conditions favoring ascending infection of the pancreatic ducts.

The causes of chronic pancreatitis just considered are such as affect the gland by way of its ducts. In a smaller group of cases the lesion is referable to the bloodvessels or to toxic substances carried to the gland by them. Arteriosclerosis causes chronic pancreatitis, according to Hoppe-Seyler and Fleiner, and the lesion is analogous to the contracted kidney and to the changes in the liver, heart, and brain following arterial disease. In a case of diabetes with calcification of the posterior tibial artery and gangrene of the foot, chronic pancreatitis, included among the 30 cases previously cited, accompanied advanced sclerosis of the pancreatic vessels; Hoppe-Seyler has recently described 9 similar cases.

Since alcohol is regarded as one of the most important factors in the production of cirrhosis of the liver, its relation to the similar lesion of the pancreas has much interest. The literature of pancreatic disease contains numerous instances in which the lesion has been found in individuals addicted to the excessive use of alcohol. Specially noteworthy is the fact that the lesion in these cases is frequently, although not necessarily, associated with cirrhosis of the liver. Factors other than alcohol producing chronic inflammation act simultaneously upon the liver and pancreas, and chronic pancreatitis and cirrhosis have been found associated by many observers, notably by Kasahara, by Lefas, and by Steinhaus.<sup>1</sup> Among 30 cases of chronic pancreatitis, in 8 cirrhosis was present.

**Pathology.**—Interest in chronic pancreatitis has in large part limited itself to the relation of the lesion to diabetes mellitus, and since it may occur with or without diabetes attempts have been made to define the peculiarities of those lesions which cause a disturbance of carbohydrate metabolism. Hansemann has described a form of chronic pancreatitis which is, he believes, peculiar to diabetes. He designates the condition atrophy, but carefully distinguishes it from simple atrophy due to cachexia, and defines it as a type of chronic inflammation resembling certain forms of granular atrophy of the kidney. In a later paper Hansemann has defined with greater detail the microscopic characters of so-called granular atrophy and states that it agrees substantially with what has been subsequently called interacinar pancreatitis.

Two types of chronic interstitial pancreatitis are distinguishable. In one type broad bands of newly formed connective tissue occupy the site of the larger trabeculae of the gland and separate the lobules or groups of lobules; areas of surrounded parenchyma are often wholly uninvaded by the sclerotic process; the lesion may be designated chronic *interlobular* pancreatitis. With the second type of chronic inflammation newly formed connective tissue does not form broad bands, but occurs diffusely scattered in small patches and strands, invading the lobules of parenchyma

<sup>1</sup> *Deutsch. Arch. f. klin. Med.*, 1902, lxxiv, 537.

and separate individual acini. The lesion may be called chronic *inter-acinar* pancreatitis. Among 30 instances of chronic pancreatitis, in 21 the lesion was of the interlobular and in 9 of the interacinar type.

*Chronic interlobular pancreatitis* results when the duct of the gland is occluded or when the inflammatory process is the result of ascending infection of the ducts. Typical interlobular pancreatitis can be produced in cats by ligation of the ducts of the gland; at the end of a week or more each lobule, which in this animal is unusually sharply defined, is separated from its neighbors by thickened bands of connective tissue. In human cases the most intense grades of pancreatic sclerosis occur with duct obstruction resulting from the presence of pancreatic calculi. The organ may be converted into a narrow band of dense scar-like tissue surrounding the moderately dilated duct filled with numerous concretions. To the naked eye the tissue of the organ altered by interlobular inflammation is firmer than usual, and on section is compact in texture, the areolar character of the interstitial tissue being lost.

At an early stage of the lesion the newly formed tissue shows little tendency to invade the lobules of the parenchyma, and in most instances only their peripheral parts contain invading strands of tissue. At a later stage entire lobules and groups of lobules are completely destroyed, so that a group of several widely separated and atrophied acini embedded in cellular interstitial tissue may be all that remains of one or more lobules. Characteristic both of the experimental and of the human lesion which follows occlusion of the pancreatic ducts is the behavior of the islands of Langerhans. Since the cells forming the islands of Langerhans have no communication with the ducts of the pancreas and take no part in the elaboration of the pancreatic juice, it is not surprising that they are less affected than the cells of the secreting acini, and often remain wholly uninjured, although the secreting parenchyma has almost completely disappeared. Since intervening acini are replaced by scar-like connective tissue, islands of Langerhans which have been previously separated are brought close together, so that in a given area their number may appear to have greatly increased. Embedded in dense, fibrous tissue, which in time undergoes contraction, the resisting islands of Langerhans finally suffer, possibly as the result of interference with their blood supply. The cells atrophy, and small groups of much atrophied cells scattered in dense stroma may be all that remains of these bodies.

With *chronic interacinar pancreatitis*, characterized by a diffuse new-growth of interstitial tissue penetrating between the acini, the organ is tough rather than hard, and does not exhibit the nodular surface seen with the interlobular type. In some instances the organ shows no noteworthy macroscopic change. The newly formed interstitial tissue is somewhat irregular in distribution, so that at one point there may be diffuse thickening of the strands of connective tissue between the acini, while elsewhere occur larger bands or masses of stroma. The interlobular tissue is not unaffected, but its proliferation is not a constant feature of the lesion, so that the lobulation of the organ is not accentuated, but rather obscured, since irregularly scattered strands of new tissue tend to obscure the interlobular boundaries.

With the interlobular type of inflammation the islands of Langerhans persist, and are affected only when the lesion has reached a very advanced stage; but with the interacinar type, on the contrary, these islands are implicated even when the lesion is little advanced. They are surrounded by fibrous tissue, which forms a capsule separating them from adjacent acini. Within the islands there may be proliferation of interstitial tissue forming coarse strands, which follow the course of the capillaries and separate the columns of epithelial cells. With increase of stroma the cells atrophy or disappear, so that the entire structure is replaced by a minute fibrous scar.

Chronic interlobular pancreatitis, in many instances at least, is referable to an irritant which attacks the glands by way of its ducts. In those instances in which the etiology of the interacinar type is evident, the exciting cause, on the contrary, seems to reach the organ by way of the bloodvessels. Where chronic inflammation is a consequence of arteriosclerosis, it is of the interacinar type; observations of Lefas and of the writer show that many cases of chronic pancreatitis associated with atrophic cirrhosis of the liver, and presumably due to the action of the same cause, which is in many instances alcohol, are interacinar. In some cases the etiology of interacinar pancreatitis is obscure.

Chronic interstitial inflammation of the pancreas, which accompanies the disease known as *hemochromatosis* (or when accompanied by diabetes mellitus as bronzed diabetes), affects the interacinar tissue and implicates the islands of Langerhans; there may be in addition some thickening of the strands of connective tissue between the lobules of the gland. The deposition of an iron-containing pigment in the liver, pancreas, and other glands is accompanied by degeneration of the parenchymatous cells and chronic interstitial inflammation of these organs. Bronzing of the skin due to deposition of pigment occurs, and in the later stages of the disease there is diabetes mellitus, which is the usual cause of death. The pancreas is firm in consistence and of a chocolate-brown color due to the presence of yellowish-brown pigment both in the parenchymatous cells and in the interstitial tissue of the organ.

**Clinical Significance of Chronic Interstitial Pancreatitis.**—Chronic pancreatitis is rarely accompanied by such definite symptoms that its diagnosis is possible, but the relation of the disease to other recognizable lesions and its association with diabetes mellitus may suggest its probable existence. Symptoms such as severe pain in the epigastrium and in the midscapular region, vomiting, and loss of weight and strength have been noted in association with chronic inflammation of the gland, but are referable with certainty to the disease which frequently accompanies grave disturbances of the stomach, duodenum, or bile passages. Disturbance of digestion due to loss of pancreatic juice and indicated by the presence of fatty stools may occur with chronic pancreatitis, but is usually the result of carcinoma, cysts, or calculi, which occlude the duct and as a consequence cause chronic inflammation.

Probable existence of chronic pancreatitis may be suggested by lesions of adjacent organs, particularly when such lesions are accompanied by glycosuria. Chronic interlobular pancreatitis is almost constantly



present in association with carcinoma of the head of the pancreas and with pancreatic calculi, but only when the lesion is advanced and partial destruction of the islands of Langerhans has occurred does diabetes mellitus ensue. Hence glycosuria is present in a relatively small proportion of instances of pancreatic lithiasis and of carcinoma of the gland, and rarely, if ever, accompanies chronic pancreatitis caused by biliary calculi. Since glycosuria in association with carcinoma, cyst, or calculi indicates far-advanced chronic disease of the pancreas, it has grave prognostic significance.

Riedel and Mayo Robson have emphasized the importance of recognizing at operation chronic interstitial pancreatitis occurring with cholelithiasis. In a certain number of operations for the relief of gall-stones the head of the pancreas is so indurated that carcinoma is suspected. In several cases a grave prognosis has been based upon the discovery of induration, but the recovery of the patient has proved the absence of malignant growth. Mayo Robson believes that chronic pancreatitis should be regarded as a serious complication of gall-stones, at times causing death with increasing weakness and emaciation; cholecystotomy with drainage of the gall-bladder and removal of the calculi, when necessary, is, he maintains, followed by recovery.

While chronic interlobular pancreatitis is accompanied by diabetes mellitus in only a small proportion of cases, and occurs only when the lesion is far advanced, chronic interacinar pancreatitis which implicates the islands of Langerhans is in almost all cases accompanied by glycosuria. The disease causes relatively slight destruction of the secreting parenchyma and is rarely accompanied by symptoms, other than glycosuria, referable to the gland. In a large proportion of cases it will be impossible to decide during life if diabetes is referable to interacinar pancreatitis. When, however, diabetes mellitus occurs in an individual suffering from cirrhosis of the liver, the former disease is with considerable probability dependent upon the coexistence of chronic interacinar pancreatitis. In another group of cases diabetes mellitus accompanied by advanced arteriosclerosis may with much probability be referred to chronic interacinar pancreatitis caused by the arterial disease.

### TUBERCULOSIS OF THE PANCREAS

Miliary tuberculosis of the pancreas in association with acute or chronic tuberculosis of other organs is not uncommon, but widespread tuberculosis causing functional disturbance or recognizable enlargement of the gland is almost unknown. Among 128 cases of tuberculosis Kudrewetsky found tubercles in the pancreas in nearly a tenth of them; they were common with acute miliary tuberculosis and with tuberculosis in children. Large tuberculous lesions are uncommon. Chvostek described a case in which the enlarged pancreas formed a fibrous mass containing caseous areas the size of a walnut. In a case described by Sendler a small tumor was felt above the umbilicus in a woman who had suffered with pain and vomiting during nine months;

a small mass removed at operation from the head of the pancreas was found to be a tuberculous lymphatic node. Carnot mentioned a case in which the splenic end of the pancreas in contact with a tuberculous kidney was the seat of tuberculosis.

### SYPHILIS OF THE PANCREAS

Congenital syphilitic pancreatitis was found by Birch-Hirschfeld in 29 of 124 syphilitic newborn infants. With this lesion increase of the interstitial tissue prevents the development of the secreting parenchyma; the islands of Langerhans resist the process better than the secreting parenchyma, and persist, surrounded by connective tissue. Miliary gummata occur occasionally within the connective tissue which has undergone proliferation. The pancreas is rarely the seat of gummata occurring as the result of acquired syphilis. From the older literature Friedreich cited three cases in which gummata of the pancreas were associated with characteristic syphilitic lesions of other organs. Cases of pancreatic syphilis in which the lesion is analogous to that of syphilis of the liver have been described by Drozda and by Schlagenhauer; in association with syphilitic lesions in other parts of the body the pancreas has been found to contain scar-like masses of connective tissue within which are caseous gummata. In a case of Chvostek the tail of the pancreas was penetrated by sclerotic bands which gave it a lobed appearance; gummata were not present. There are no data with reference to the symptoms or diagnosis of syphilis of the pancreas.

### CALCULI OF THE PANCREAS

Pancreatic calculi occur much less frequently than gall-stones, which in most instances are formed within the gall-bladder, and not like pancreatic stones within ducts. Two instances occurred among 1500 autopsies at Johns Hopkins Hospital. Unlike gall-stones, pancreatic calculi occur more frequently in men than in women; among 57 cases collected from the literature by Lazarus,<sup>1</sup> 47 were in men and 10 in women, a ratio of about 5 to 1. In almost two-thirds of these cases the disease affected individuals between the ages of thirty and fifty years.

**Etiology.**—The presence of calculi is usually associated with acute and chronic inflammatory changes in the ducts and in the parenchyma of the gland, but etiological relation of these factors to lithiasis is doubtful, since, in part at least, they are caused by occlusion of the ducts or by secondary invasion of bacteria. Giudiceandrea was able to demonstrate the colon bacillus together with numerous long bacilli within pancreatic calculi, while in a second case he found in the centre of a calculus numerous cocci and bacilli.

The association of pancreatic and biliary calculi in a considerable number of cases cited by Ancelet (eight cases), and observed by Curnow,

<sup>1</sup> *Beiträge zur Pathologie und Therapie der Pankreaserkrankungen*, Berlin, 1904.

Dieckhoff, and Lazarus, suggests the possibility that ascending affection from the bile passages, favored perhaps by temporary obstruction of the pancreatic ducts by passing gall-stones, may have caused pancreatic lithiasis, although perhaps both biliary and pancreatic calculi may have been due to the same cause. That stagnation of pancreatic secretion favors the formation of calculi is indicated by cases in which calculi, at times in considerable number, are found within pancreatic cysts. Occasionally an impacted stone has caused the formation of a retention cyst, but in other cases large cysts of obscure origin have contained numerous calculi; Lazarus has observed 4 such cases.

**Pathology.**—In some cases the pancreatic ducts contain fine sand-like concretions, but more frequently several stones, perhaps a centimeter or more in diameter, are present. The largest recorded calculus (Schuppmann) was stellate in shape and measured one and a half inches in its largest diameter. A solitary calculus is rarely found, while several hundred varying greatly in size may be present. In some instances projections from a large stone situated in the large duct extend into adjacent branches, so that a cast of the dilated ducts is produced. In consistence pancreatic concretions vary considerably, being at times mortar-like and friable, but usually hard; they may have a nucleus of organic material consisting of cell detritus. Pancreatic calculi are white, often grayish or yellowish white, but in rare instances black or brownish-black concretions have been found within the ducts.

Biliary calculi have in several cases been found within the duct of Wirsung near its junction with the common bile duct. In an example of suppurative pancreatitis, described by Dieckhoff, the duct of Wirsung was dilated and contained a gall-stone.

Pancreatic calculi are composed in great part of inorganic salts, of which calcium carbonate and calcium phosphate are most abundant, although sodium phosphate, magnesium phosphate, and other salts may be present. Calculi consisting almost wholly of calcium carbonate or calcium phosphate have been described. The composition of calculi from two cases described by Johnston<sup>1</sup> was as follows: (1) Calcium phosphate, 72.3 per cent.; calcium carbonate, 18.9 per cent.; organic matter, 8.8 per cent. (2) Calcium carbonate, 91.65 per cent.; magnesium carbonate, 4.15 per cent.; organic matter, 3 per cent. In most instances inorganic constituents are more abundant than organic material, but in a case described by Baldoni organic material formed the greater part of the concretion. A calculus having a nucleus of calcium carbonate surrounded by a layer of cholesterin has been described by Freyhan. A calculus consisting of calcium oxalate has been found at operation in a pancreatic cyst by Shattuck.<sup>2</sup>

Calculi may be situated in the larger ducts or their branches, but calculi of considerable size are usually found in the duct of Wirsung, of which the lumen is frequently so completely occluded that outflow of secretion is prevented and dilatation behind the obstruction results. Stones embedded in ampulla-like diverticula of the large duct have been

<sup>1</sup> *Amer. Jour. Med. Sc.*, 1883, lxxvi, p. 404.

<sup>2</sup> *Brit. Med. Jour.*, 1896, i, 1034.



described. Since the duct of Wirsung is narrower near its duodenal orifice than elsewhere, calculi tend to lodge in this situation, and the duct may be uniformly dilated to a diameter of a centimeter or more. Stones lodged in the terminal part of the duct of Wirsung may compress the common bile duct and cause jaundice; Gould found in the diverticulum of Vater a pancreatic calculus which had caused jaundice.

Obstruction to the outflow of pancreatic juice, doubtless in association with bacterial infection, causes chronic interstitial inflammation of the pancreas, which may reach such an advanced stage that the gland is converted into dense fibrous tissue surrounding the dilated duct, secreting parenchyma having almost completely disappeared. The most intense sclerosis occurs in association with calculi. In the contracting fibrous tissue the islands of Langerhans finally undergo changes, being compressed and invaded by the sclerotic tissue. In cases of diabetes with pancreatic lithiasis the islands of Langerhans had suffered similar changes (Lazarus, Pearce, Lancereaux, etc.).

Calculi situated within the ducts not infrequently cause ulceration of the mucosa by pressure. In the immediate neighborhood of a stone chronic inflammation more intense than elsewhere may produce abundant scar tissue, distorting the duct. The presence of bacteria may result in pancreatic *abscess*, not an infrequent result of pancreatic calculi.

**Symptoms.**—Pancreatic lithiasis may be unaccompanied by noteworthy local symptoms indicating disease of the organ. Lazarus described such a case in which death occurred with diabetes and pulmonary tuberculosis. At autopsy the pancreas was found to be converted into a fibrous sac and notwithstanding the fact that the duct contained numerous jagged concretions, there had been no pain.

The most frequent symptom is *pain*, which may be continued or intermittent; in some instances there is merely a sense of pressure. More characteristic are attacks of colicky pain, which in some instances have been regarded as sufficiently distinctive for diagnosis. Friedreich doubted the occurrence of *pancreatic colic* analogous to gall-stone colic. Subsequent observations have shown that severe attacks of colic-like pain occur in association with the passage of calculi. In a case of Leichtenstern's, symptoms of biliary colic without jaundice were followed by the passage with the feces of three concretions, the largest the size of a pea; analysis showed that they were composed of calcium carbonate without traces of either bile pigments or cholesterin. Pain has been localized in the epigastrium and under the left costal margin in the mammillary line, radiating on the left side to the spine or to the left shoulder-blade. Pain with pancreatic lithiasis does not necessarily occur to the left of the midline, but may be limited to the region of the epigastrium or of the umbilicus, or may even radiate to the right side (Eichhorst).

As with biliary colic, the attacks of pain associated with passage of pancreatic calculi are often accompanied by vomiting. Reflex circulatory disturbances, such as weak pulse and temporary collapse, may occur. The pain is at times accompanied by a chill which is followed by fever, possibly referable to bacterial invasion of the occluded duct.

The passage of a pancreatic calculus through the diverticulum of

Vater may cause temporary *jaundice*. A patient of Leichtenstern suffered during two years with attacks of a severe abdominal pain accompanied by vomiting and on one occasion by jaundice, but cholecystotomy undertaken for the relief of gall-stones demonstrated their absence; autopsy showed the presence of numerous pancreatic calculi. The relatively frequent association of cholelithiasis with pancreatic lithiasis may explain the occurrence of jaundice in some instances.

In several instances a diagnosis of pancreatic lithiasis has been made during life from the passage with the feces of calculi composed of calcium carbonate or phosphate and free from bile pigments or other constituents of the bile. In a case of Minnich during twelve days following an attack of colic, soft friable concretions as large as a cherry pip were found, containing carbonate and phosphate of calcium.

*Diabetes mellitus*, or alimentary glycosuria, has been a symptom of pancreatic lithiasis in a large proportion of the recorded cases; Lazarus has collected 80 cases, among which glycosuria occurred in 36 (45 per cent.). Pancreatic lithiasis is an infrequent cause of diabetes, occurring only 5 times among 288 cases of diabetes recently collected from the literature. Pancreatic lithiasis may exist for years without diabetes, and in the case described by Caparelli glycosuria appeared six years after the first attack of colic. Since glycosuria is not the result of occlusion of the pancreatic ducts but of consequent chronic interlobular inflammation, diabetes results only after the lesion has become far advanced and has injured the islands of Langerhans. At one stage of the disease the organ is subject to such slight impairment of function that *alimentary glycosuria* occurs; in the cases of Lichtheim, Lazarus, and Opie, glycosuria disappeared when the patient was given a diet poor in carbohydrates. In the cases of Polyakoff and of Minnich transient glycosuria occurred only after attacks of colic, and was doubtless analogous to that which not infrequently follows experimental injury to the gland, insufficient to cause permanent diabetes.

*Steatorrhœa* has been present in 10 of the cases collected by Lazarus. In the table of Fitz, which contains 29 cases in which visible fatty stools have accompanied demonstrable pancreatic disease, pancreatic lithiasis was present in 7 instances. In none of the cases of Fitz was jaundice present, while in 4 there was glycosuria. In cases studied by Müller and by Kinnicutt and Herter, although fat was not visible in the feces, chemical analysis demonstrated that the percentage of split fat was much less than normal. *Azotorrhœa*, shown by the presence of undigested muscle fibres in the feces, is even less common than fatty stools, and in only one (Lichtheim) of the eight instances in which this symptom accompanied well-authenticated pancreatic disease (Fitz) was the pancreatic lesion caused by calculi.

The *loss of weight* in association with pancreatic lithiasis in the absence of diabetes or disturbances of digestion is probably referable, in part at least, to inflammatory changes or other complications of the disease.

**Complications.**—Among these the most frequent and serious is *abscess*. Rupture may occur into the peritoneal cavity causing a localized bursal abscess or fatal general peritonitis. A fistulous communication with the

intestinal tract may be formed; in a case described by Nicholas and Mollière one liter of blood was passed by rectum two and a half months after an attack of severe epigastric pain; a second attack of colic and subsequent hemorrhage, together with chills, fever, and glycosuria, preceded death. The duct of Wirsung contained about twenty concretions, while in the substance of the gland communicating by a fistulous opening with the duodenum was an abscess from which hemorrhage had occurred. In the case of Caparelli an abscess opened near the umbilicus, and calculi were passed from the fistula which persisted for six years.

The association of cysts with pancreatic calculi has already been mentioned. Cases in which *carcinoma* of the pancreas has been described in association with calculi date from a time when chronic inflammation was not infrequently mistaken for scirrhus carcinoma. In a case of Schupmann carcinoma occupied the tail of the gland, and in the region of the tumor within the duct was a large jagged concretion.

**Diagnosis.**—Kinnicutt collected from the literature seven cases in which a diagnosis of pancreatic lithiasis was made during life. In the case of Caparelli calculi were discharged from a fistula in the epigastric region, and in the cases of Leichtenstern, Minnich, and Kinnicutt calculi consisting of phosphate or carbonate of calcium without mixture of bile salts were passed with the stools after attacks of epigastric colic. An additional case has been described by Cipriani.<sup>1</sup>

A review of the recorded cases gives no data by which it is possible to distinguish pancreatic from biliary colic, although localization of the pain below the left costal margin may be suggestive of pancreatic lesion. Diabetes mellitus, or alimentary glycosuria, may indicate a lesion of the gland. Fatty stools have been less frequently observed, and in the absence of jaundice have diagnostic value; diminution of split fat in the feces is believed to have similar significance. Jaundice may be caused by a pancreatic calculus lodged in the diverticulum of Vater, or by biliary calculi, which occur with relative frequency in association with pancreatic calculi, and does not exclude pancreatic colic.

**Treatment.**—Statements concerning this are necessarily vague, since few cases have been recognized during life. Attacks of colicky pain have been treated by sedatives applicable to biliary colic. Measures which increase the flow of pancreatic juice have been suggested for the purpose of overcoming obstruction to its outflow, particularly since duct obstruction is believed to be an important factor in the production of calculi. Physiological observations according to Lazarus suggest that this may be accomplished by water in abundance, especially when carbonized or acidified by other means; alkalis are thought to diminish pancreatic secretion. To increase the flow of pancreatic juice, Eichhorst injected pilocarpine subcutaneously in a case believed to be pancreatic lithiasis, and found that attacks of colic disappeared. It is noteworthy in this connection that pilocarpine administered to animals with the pancreatic ducts ligated caused necrosis of almost the entire abdominal fat, and death within four days.

<sup>1</sup> *Amer. Jour. Med. Sc.*, 1902, cxxiv, 948.



The presence of glycosuria indicates that the pancreas has undergone grave sclerotic change; nevertheless, in several instances with diabetic diet the sugar has disappeared.

Analogy with gall-stones suggests the possibility of surgical treatment. Gould<sup>1</sup> found at operation upon a patient suffering with symptoms of cholelithiasis a lump at the posterior part of the lesser peritoneal cavity, and on incision removed a calculus from the duct of Wirsung. Obstruction to the flow of bile was not relieved, and at a second operation a stone was removed from the head of the pancreas; although bile subsequently entered the intestine, death occurred as the result of suppuration twelve days later. Moynihan<sup>2</sup> removed through the duodenum a calculus lodged in the duct of Wirsung and projecting into the diverticulum of Vater. Straehlin and Roeber<sup>3</sup> cut into the head of the pancreas and successfully removed several calculi from the duct of Wirsung.

### CYST OF THE PANCREAS

Varieties of lesions are described as cysts of the pancreas; their common character is the presence in the upper part of the abdominal cavity of an encapsulated collection of fluid in contact with the gland and apparently derived wholly or in part from it. Since the greater number of such cysts are observed at operation, the exact nature of the disease is often obscure and its relation to the pancreas is not always established, particularly because fluid encapsulated by the thickened wall of the bursa omentalis may produce signs indistinguishable from those of pancreatic cysts situated within the substance of the gland.

**Classification.**—True cysts derived from the ducts or acini of the pancreas and lined by a layer of epithelial cells have been distinguished from so-called pseudocysts, which have walls of thickened connective tissue and are without epithelial lining. True cysts may be formed by dilatation of the pancreatic duct or its branches due to obstruction, and are retention cysts, or may be the result of spontaneous proliferation of epithelial structures, and are tumors. Pseudocysts are the result of trauma or of degenerative changes within the substance of the gland, and frequently contain blood or blood mixed with products of pancreatic secretion; pseudocysts may be situated wholly within the substances of the pancreas, or, when associated with rupture of the anterior surface of the gland may be limited in part by the walls of the bursa omentalis. Pseudocysts, it has already been shown, may be the result of acute hemorrhagic pancreatitis. The etiology and course of these diverse lesions vary so greatly that it would be desirable to consider them separately were they not characterized by certain physical signs common to all encapsulated collections of fluid having their origin in the pancreas. The relation of different parts of the pancreas to adjacent structures determines the location of such cysts and the point at which they present

<sup>1</sup> *Lancet*, 1898, ii, 1632.

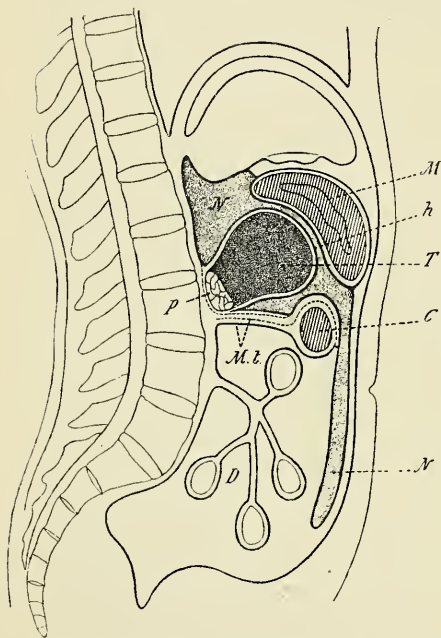
<sup>2</sup> *Ibid.*, 1902, ii, 355.

<sup>3</sup> *New York Med. Jour.*, 1905, lxxxiii, 904.

upon the surface of the body. From an analysis of 133 cysts upon which operation had been performed Körte described the various positions.

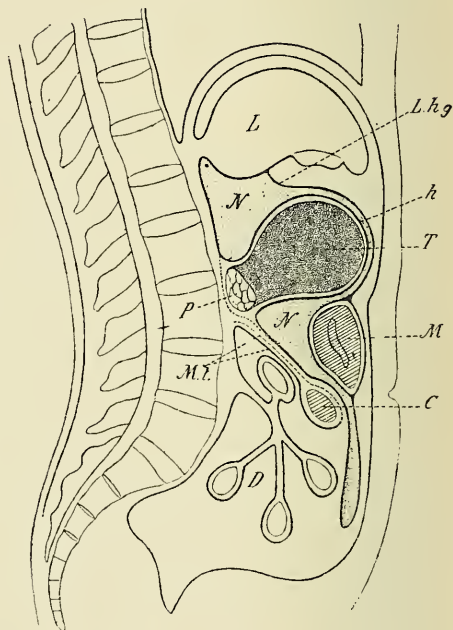
A. In the majority the cyst grows directly forward, and, pushing the stomach upward, comes in contact with the anterior abdominal wall between the stomach and colon; in order to reach the tumor at operation it is necessary to cut through the gastrocolic omentum. The cyst occupies and distends the cavity of the bursa omentalis, and, stretching the gastrocolic ligament, may, with increased growth, push downward the transverse colon so that it may reach the symphysis pubis. Pseudocysts which arise from the pancreas and, as the result of rupture of its overlying

FIG. 6



Cyst projecting into the lesser peritoneal cavity behind the stomach and above the colon. (Oser.)

FIG. 7



Cyst projecting into the lesser peritoneal cavity, and in contact with the abdominal wall between the stomach and pancreas. (Oser.)

peritoneum, communicate with the bursa omentalis, and are in large part limited by this cavity, occupy the position described and present upon the surface of the abdomen between stomach and colon. Jordan Lloyd has shown that accumulations of fluid in the lesser peritoneal cavity due to a variety of causes may closely resemble these cysts of the pancreas. The stomach is compressed and flattened, but usually pushed upward. Should adhesions be formed between the cyst and the stomach, the latter may be held in front of the tumor and drawn downward by it.

B. Less frequently the cyst makes its way above the lesser curvature of the stomach between the stomach and liver, stretching the gastro-

hepatic omentum which covers it. The upper border of the pancreas is at a higher level than the lesser curvature of the stomach, so that a cyst arising from this part of the gland may present above the stomach, which, with further growth of the tumor, is pressed downward; with gastropptosis the extent of pancreas above the lesser curvature of the stomach is increased. Körte cites 9 cases in which the cyst presented at operation above the stomach, and in 2 cases described by Riegner and Finotti a diagnosis of the position was made.

FIG. 8

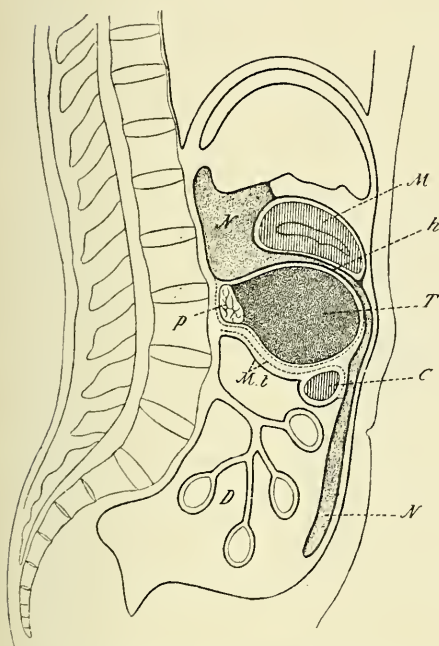
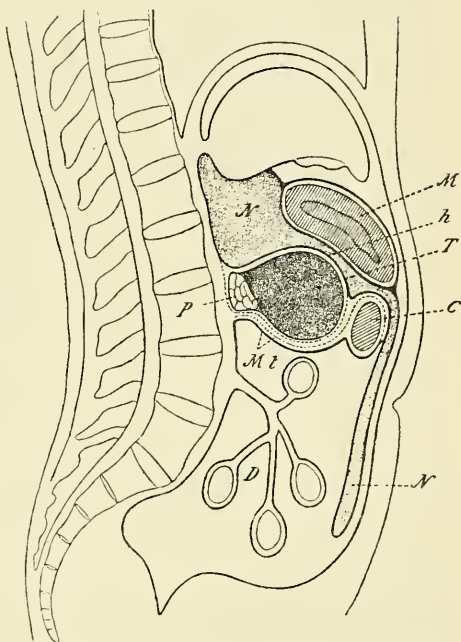


FIG. 9



Cyst projecting from the upper surface of the mesocolon and presenting between stomach and colon. (Oser.)

Cyst occupying position of mesocolon, with colon overlying. (Oser.)

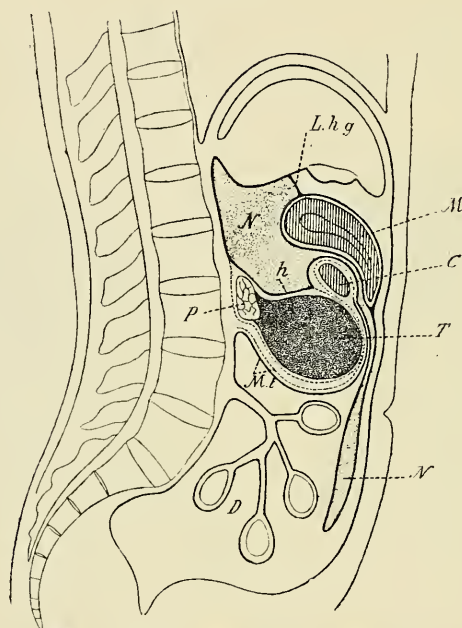
C. In a third group the cyst in growing penetrates the layers of the mesocolon. Growth into the mesocolon is more likely to occur when the cyst is situated toward the tail of the gland, since this part of the organ is situated between the layers of the mesocolon; the head of the pancreas being situated in the loop formed by the duodenum, cysts from this part do not find their way into the mesocolon. Körte cites 7 instances in which the cyst situated in the mesocolon pushed forward the upper layer of the membrane and reached the anterior abdominal wall between the stomach and colon. The transverse colon may be forced downward to the pelvis, and the descending colon may overlie the tumor. In 3 instances the cyst projected upon the under surface of the membrane, so that the transverse colon was found upon its upper margin. Lazarus mentions an intermediate position in which the cyst distends the upper



and lower layers of the mesocolon equally so that the transverse colon is found to cross the summit of the tumor.

A case described by Dreyzehner, according to Lazarus,<sup>1</sup> does not belong to any of the groups already defined; this type may be designated prevertebral. A tumor arising from the head of the pancreas forced its way behind the peritoneum to the right of the midline and displaced the right kidney. Payr<sup>2</sup> described a cyst of the pancreas which was found at operation within the larger peritoneal cavity between the liver and pancreas; it had made its way through the foramen of Winslow.

FIG. 10



Cyst projecting from lower surface of the mesocolon and presenting below the colon. (Oser.)

**Etiology and Pathology.**—Cysts of the pancreas occur with approximately equal frequency in males and in females. Railton has described an instance of pancreatic cyst occurring in an infant six months old, and Shattuck found a cyst of the gland in a boy thirteen months old. About half the cases occur between the ages of twenty and forty years.

**Retention Cysts.**—Cysts formed as the result of obstruction of the larger pancreatic ducts or their branches, designated retention cysts, are often of small size and unaccompanied by clinical symptoms. Under the name of *ranula pancreatica* Virchow described dilatation of the duct of Wirsung due to occlusion caused by a villous tumor of the duodenum; the duct had numerous sacculations, giving it a beaded appearance.

<sup>1</sup> *Beiträge zur Pathologie und Therapie der Pankreaserkrankungen*, Berlin, 1904, and *Zeit. f. Heilk.*, 1901, xxii, 165.

<sup>2</sup> *Wiener klin. Woch.*, 1893, xii, 629.

Klebs described as *acne pancreatica* multiple small cysts containing fluid, sometimes clear and sometimes opaque, yellowish, and thick.

Ligation of the ducts of the pancreas causes only slight dilatation of the occluded channels, and is followed by chronic inflammation of the gland. Complete obstruction to the outflow of secretion in man is usually followed by similar changes. It has been thought that partial or intermittent occlusion may cause cysts. Cysts of the pancreas apparently due to retention of pancreatic secretion have been found associated with obstruction of ducts due to a variety of causes, but the conditions which favor their formation are not understood. Cysts of large size have been found in association with pancreatic calculi. von Recklinghausen found, with a cyst almost the size of a child's head, the duct of Wirsung occluded by a calculus. Lazarus found calculi in the contents of pancreatic cysts in 2 of 14 cases, but suggests that the cyst may afford conditions which favor the formation of concretions.

The walls of pancreatic cysts are usually several millimeters in thickness and are composed of dense fibrous tissue in which remains of pancreatic parenchyma may be found. The inner surface may be smooth and lined by a single layer of cylindrical cells. The presence of such cells indicates the cyst has had its origin in a dilated duct.

**Proliferation Cysts.**—The occurrence of multilocular cysts of the pancreas, the presence of numerous small cysts in the wall of a large cyst, or the presence of papillary projections upon the inner surface have been regarded as evidence that cysts may be formed by proliferation of epithelial tissue of the gland. In some instances cysts of the pancreas resemble the cystadenomas of the ovary and other organs, and have been regarded as true tumors. Fitz<sup>1</sup> described a multilocular cystoma which apparently had its origin in the pancreas, and collected 9 somewhat similar cases from the literature; 8 cases occurred in women, and in most instances the growth existed for a number of years without causing severe inconvenience. In no case was there evident obstruction of ducts, but a description of some of the cysts does not exclude the possibility that they may have been due to occlusion of small ducts. Körte collected from the literature only 13 instances of proliferation cysts (cystadenomas); Munzer<sup>2</sup> (1903) cites 5 additional cases. In two cases cysts have been associated with malignant growths.

**Traumatic Cysts.**—Since many cysts of the pancreas contain blood the relation of cyst formation to hemorrhage into the gland has been much discussed, and so-called apoplectic cysts have been described. Hemorrhage may occur into a preformed cyst, and the presence of blood does not indicate that the lesion is the result of hemorrhage. Nevertheless, there is abundant evidence that injuries which cause local hemorrhage may result in the formation of cysts. Lazarus has shown that a small hematoma may be formed by crushing the exposed pancreas of the dog; at the end of a week the extravasated blood may have undergone encapsulation by fibrous tissue. By crushing the pancreas of a dog he caused the formation of a hematoma about the size of a pigeon's egg which, after

<sup>1</sup> *Amer. Jour. Med. Sc.*, 1900, cxx, 184.

<sup>2</sup> *Cent. f. d. Grenzgeb. d. Med. u. Chir.*, 1903, vi, 490, 529, 573, 619, 664.

forty days was converted into a cyst with a smooth, fibrous capsule containing 100 cc. of watery fluid. Lazarus thought that the hematoma, together with injured tissue and adjacent parenchyma, had undergone digestion by the secretion of the gland, while a reactive inflammation at the periphery of the lesion had resulted in the formation of a capsule, which in turn prevented the resorption of the fluid contents.

Among 117 cases of pancreatic cyst, Körte found 33 (28 per cent.) in which trauma had preceded the appearance of a cyst; Lazarus has collected 8 additional cases more recently published. In the greater number the epigastric region or the upper left quadrant of the abdomen had been the seat of the injury; in several cases there had been compression of the body or a wheel had passed over it. A violent blow from a fist or the kick of a horse has preceded the appearance of a cyst. Repeated injury of less severity has been cited as the cause of the lesion; energetic massage is mentioned by Gussenbauer.

The contents of many cysts which have followed traumatism are bloody, but not infrequently such cysts have contained clear fluid free from blood. The demonstration of one or more ferments either in the contents of the cyst or in the fluid escaping from a fistula after operation has been cited as evidence of connection with the pancreas. Drainage of the cyst has usually been followed by recovery, and in only a few instances have these cysts been studied at autopsy. In the case of Richardson the pancreatic duct communicated with the cyst. Jordan Lloyd has maintained that accumulations of fluid in the lesser peritoneal cavity following contusions of the upper part of the abdomen are often mistaken for true cysts of the pancreas. In a case which he recorded fluid removed at operation had the power of rapidly converting starch into sugar, and was derived in part, he believed, from the injured pancreas.

A number of cases furnish evidence that cysts may follow acute hemorrhagic pancreatitis. The pathogenesis of the lesion doubtless resembles that of traumatic cysts. Hemorrhagic and necrotic tissue undergoes partial solution and subsequent encapsulation by fibrous tissue.

**Contents.**—These vary greatly, being in many instances mixed with fresh or altered blood. Occasionally clear and watery in appearance, more frequently the fluid is viscid, and in several instances the presence of mucus has been demonstrated. In most instances hemorrhage has occurred into the cyst, and while occasionally the contained fluid may appear to be pure blood, subsequent changes, due in part to the action of digestive ferments, may produce a greenish, brownish, coffee-colored, or even black fluid.

Much significance was formerly attached to the presence of ferments resembling those of the pancreatic secretion, but the absence of one or more of these ferments in the contents of pancreatic cysts and the presence of similar ferments in cysts of other organs has greatly diminished their diagnostic value. The presence of tryptic, diastatic, and emulsifying ferments may suggest the character of fluid removed by operation, but rarely is it possible to demonstrate all three ferments, while most frequently the diastatic ferment alone can be found. The antitryptic



action of the blood serum may explain occasionally the absence of trypsin in cysts with hemorrhagic contents. Only when the cyst is in communication with the secreting parenchyma can the ferments of the gland find their way into its contents, while observation on animals (Heidenhain) shows that the secretion of the chronically inflamed pancreas may contain little, if any, ferment.

Fat-splitting, diastatic, or proteolytic ferments, moreover, have been demonstrated in a variety of fluids which do not have their origin in the pancreas. Since Körte has found a weak diastatic ferment in the contents of a mesenteric cyst, he thinks that fluid from a cyst must exhibit active diastatic action in order to suggest a probable pancreatic origin. Boas thinks that tryptic ferment is characteristic of these cysts, but Lazarus has found a fibrin-digesting ferment in the contents of an ovarian cyst, and it is probable that any fluid containing leukocytes in considerable number will exert proteolytic action in an alkaline medium.

**Symptoms.**—A rounded tumor fluctuating on palpation and situated in the epigastric region behind the stomach and in greater part to the left of the median line suggests the presence of a pancreatic cyst, but the variation to which these characters are subject often makes recognition of the tumor difficult. In the majority of cases the tumor is situated between the ensiform cartilage and the umbilicus, and may produce a rounded protrusion of the abdominal wall. In 48 cases collected by Körte the tumor occupied the median line; in 40 instances the greater part of the mass was to the left of the median line, extending to the left costal margin, and in some instances into the lumbar region. In only 10 cases was the larger part of the cyst to the right of the median line. Very large tumors extend into the lower part of the abdominal cavity, and in 16 cases the tumor extended below the level of the umbilicus, sometimes as far as the symphysis pubis.

The size of the cyst is subject to equal variation; in many instances it is described as the size of a man's head, but may distend the abdominal cavity, extending from the ensiform process to the symphysis pubis. In shape the cyst is usually spherical and the surface is smooth. Fluctuation can usually be felt, but rarely the fluid contents have distended the sac so tensely that the tumor has appeared to be solid. When the cyst is grasped between the hands, one placed upon its abdominal surface, the other upon the lumbar region, pressure of one hand is transmitted to the other. Pancreatic cysts, contrary to the statements of some writers, are not infrequently *movable*, and, particularly when in contact with the diaphragm, move with respiration. Cysts arising from the tail of the gland are particularly movable, and unless fixed by adhesions can be pushed both from above down and laterally. Cysts which lie in front of the aorta may, when sufficiently tense, transmit its pulsation, but cease to pulsate when the patient is in the knee-chest position.

Of much importance is *the relation of the cyst to adjacent organs*, and especially to the stomach and colon, between which in most instances it reaches the abdominal wall. Small cysts may be wholly covered by the stomach, but with increase of their size the organ is pushed upward, so that when artificially distended its tympany separates the dulness

produced by the cyst from that of the liver. The colon, best mapped out after inflation with air, is found along the lower border of the cyst, being in some instances pushed downward to the symphysis pubis. When the cyst occupies the mesocolon, the colon may be below the tumor, may cross its summit, or lie along its upper border in accordance with the previously described relation which the cyst bears to the upper or lower surface of the membrane. When the cyst projects upon the lower surface of the mesocolon, the tumor may occupy the lower part of the abdominal cavity, with its margin in contact with the symphysis pubis. Cysts which force their way between the liver and the stomach produce dullness in contact with that of the liver while their lower part is covered by the stomach, which, when distended, almost completely covers the tumor.

Sudden *disappearance of the tumor* of a pancreatic cyst may be the result of rupture into the peritoneal cavity. In some instances rupture has followed puncture undertaken for the purpose of diagnosis, or, as in the cases of Halsted and of Schwartz, has followed injury the result of a fall. Of greater interest is the spontaneous disappearance accompanied by temporary diarrhœa of a peculiar character, suggesting that the contents of the cyst have been discharged into the duodenum. Disappearance of the tumor in the cases of Bull and of Karewski was accompanied by the appearance of dark-colored masses in the stools. In the case described by Parson the sudden disappearance of a tumor the size of an orange situated in the epigastrium was followed by profuse whitish diarrhœal discharge; a second tumor appeared in the lower part of the abdomen at the end of several weeks, disappeared with profuse diarrhœa, and again returned. A large cyst in the epigastrium, described by Payr, disappeared with occurrence of diarrhœal discharges containing whitish particles three times during two months. The conditions which cause the periodic discharge of the cystic contents have not been explained.

*Pain* is one of the most constant symptoms, and is not infrequently present before a tumor is demonstrable. In a few instances the presence of the tumor has been unaccompanied by pain, or has merely caused a feeling of distension. Pain is usually deeply seated in the epigastric region, or may be referred to the small of the back. In some instances it has been referred to the right or left hypochondrium in accordance with the localization of the cyst in the head or tail of the gland, but little reliance can be placed upon these subjective symptoms. The intensity of the pain varies greatly. It may occur in paroxysms which in some instances have the character of gastric crises, and may be accompanied by vomiting and collapse.

Various symptoms have been produced by the *pressure of the growing cyst upon adjacent organs*. Most constant are those referable to the stomach, which in some instances is flattened by the tumor. Discomfort after eating, loss of appetite, vomiting, and other symptoms of disturbed digestion are present, and may have long preceded other evidence of disease. Compression of the intestine may be accompanied by colicky pain and constipation. In a case of Lazarus the transverse colon situated along the lower margin of the tumor was frequently the

seat of colic, and in four cases collected from the literature by this author complete intestinal obstruction had occurred.

Cysts situated in the head of the pancreas may cause *jaundice*. The relative infrequency of this symptom is explained by the fact that cysts occur more frequently in other parts of the gland. Retention cysts caused by tumors or by biliary calculi compressing the pancreatic duct are accompanied by jaundice due to the same cause.

Compression of the portal vein may be followed by *ascites* and by the establishment of collateral circulation. Dilatation of the mesenteric veins and vessels upon the surface of the cyst adds to the danger of puncture. Compression of the vena cava has been accompanied by oedema of the lower extremities. In two instances (Dreyzehner, Reeve) one ureter has been obstructed.

*Functional disturbance* of the pancreas has been noted with only a small proportion of the described cases, but careful chemical observation of the feces and tests for alimentary glycosuria would probably disclose their presence in a larger proportion. Cysts in the body or tail of the pancreas do not so readily cause such disturbances as the rarer cysts which arise from the head of the gland, since they do not occlude the large duct, and therefore do not cause chronic inflammation of the entire organ. Among 29 instances of *steatorrhœa* accompanying well-authenticated disease of the pancreas collected by Fitz the symptom was referable to cysts in only 2 cases (Bull, Goodman), in both of which diabetes was present as well. In some cases disturbance of protein digestion was indicated by the presence of undigested muscle fibres in the feces.

*Diabetes mellitus* results from the presence of cysts only when the gland is the seat of advanced chronic interstitial inflammation. Diabetes is, however, rarely present. It occurred in only 9 of 134 cases collected by Oser. Alimentary glycosuria in association with pancreatic cyst has been observed in a case described by Lazarus.

*Loss of weight* and weakness commonly accompany pancreatic cysts and may be referred in part to the digestive disturbances and vomiting caused by the pressure of the tumor. Lazarus thinks that the cause of cachexia is more obscure, and in several instances has seen loss of weight, although there was no disturbance of digestion, no diabetes, and no jaundice. One of his patients, a healthy man who developed a cyst in consequence of traumatism, became much emaciated, but after operation recovered so quickly that within six weeks he had regained fifteen pounds.

**Diagnosis.**—Recognition of pancreatic cysts depends almost wholly upon physical signs, although in a comparatively small number of cases diabetes or *steatorrhœa* confirms the diagnosis. The presence of fluctuation may serve to distinguish cysts from solid tumors of the pancreas or of retroperitoneal structures, but with cysts so tensely distended that this sign is absent some uncertainty may exist, although the spherical shape and smooth surface may indicate the character of the lesion. In determining the origin of such a tumor, of greatest significance is its relation to the stomach and colon, behind which it is situated. This is done best by percussion after inflation. In some instances information is obtained by noting the change in position of the stomach during the



progress of inflation; as the organ enlarges, it gradually overlaps an increasing area at the upper or lower margin of the tumor, in some instances completely covering it. The difficulty of diagnosis is greatest with those unusual cysts which present above the stomach or along the lower margin of the colon, the typical position being between stomach and colon and behind both.

Possible etiological factors may have an important bearing upon diagnosis. A history of injury in the epigastric region may suggest the presence of a pancreatic cyst of traumatic origin. Symptoms of hemorrhagic pancreatitis may precede the appearance of a tumor mass.

Since cysts of the pancreas may occupy almost any part of the abdominal cavity, their differential diagnosis presents many difficulties. Cysts may occur in the liver, spleen, mesentery, omentum, ovaries, retroperitoneal tissue, and adrenals, while a distended gall-bladder or hydronephrosis may resemble a cyst of the pancreas.

*Echinococcus cysts of the left lobe of the liver* may form large, fluctuating tumors in the epigastric region. The dullness produced by pancreatic cysts occupying their usual position between the stomach and colon is separated by the tympany of the former organ from the area of hepatic dullness, but should the cyst present between liver and stomach, diagnosis is more difficult. The stomach, particularly when distended, is found in front of the pancreatic tumor, which is pushed backward and becomes less palpable, but the organ cannot bear the same relation to a hepatic cyst which lies in contact with the abdominal wall. Should the cyst be punctured, the well-known hooklets, or perhaps particles of the chitinous layer of the cyst wall, may be found in an echinococcus cyst. The *distended gall-bladder*, situated in the usual position of this organ, has the respiratory movement of the liver, and, lying in contact with the abdominal wall, is rarely covered by the stomach or intestine. Cysts of the head of the pancreas, suggesting a distended gall-bladder, may be accompanied by jaundice.

*Cysts of the mesentery* have usually been found in the neighborhood of the umbilicus, and, unless fixed by adhesions, are movable in both vertical and horizontal directions. Cysts of the mesocolon are indistinguishable from similarly situated cysts of the pancreas.

The diagnosis between *ovarian cysts* and pancreatic cysts is in most instances made with little difficulty. Pancreatic cysts which arise from the tail of the gland and are situated in the mesocolon lie in contact with the pelvis and may closely simulate ovarian cysts, while cysts of great size distending the abdominal cavity may offer the same difficulty. In some instances the tumor has been first observed in the epigastric region, from which it has subsequently extended downward. Bimanual examination by vagina and rectum of an ovarian cyst may demonstrate a pedicle connecting it with the uterus and perhaps dragging the latter upward. With pancreatic cysts the uterus occupies its normal position, and the ovaries are often palpable. Pancreatic cysts of great size are situated behind the stomach and colon, while ovarian cysts push these organs upward.

Pancreatic cysts may closely simulate *hydronephrosis*. The history

indicating that the tumor has had its origin in the epigastrium may suggest pancreatic cyst. The tumor of hydronephrosis fills the lumbar region and can be forced even farther backward by distending the colon; pancreatic cysts, as a rule, do not extend beyond the axillary line behind which there is tympany. Periodic disappearance of the tumor may occur both with hydronephrosis and with pancreatic cyst, but abundant flow of urine or simultaneous onset of diarrhœa may suggest one or other condition.

Since pancreatic cysts when tensely distended have been known to transmit pulsations from the aorta, *aortic aneurism* may be suspected. The tumor rises and falls, but has no expansile pulsation; in the knee-chest position pulsation disappears.

**Treatment.**—Cysts of the pancreas have been treated by puncture, by extirpation, and by incision and drainage. Puncture followed by aspiration has proved an ineffectual and dangerous procedure. Kuster and Lazarus have mentioned the occurrence of hemorrhage into a cyst due to puncture of enlarged vessels in the wall. When the cyst is infected, purulent, general peritonitis may follow puncture. Removal of cystic contents by aspiration is usually followed by reaccumulation of fluid, even when the cyst is of traumatic origin and has walls which are not lined by epithelium.

Complete extirpation of a pancreatic cyst was successfully performed in 1882 by Bozemann. The operation is difficult and dangerous, on account of the close proximity of important bloodvessels, and may be followed by diabetes mellitus when a considerable part of the gland is removed. The operation is rarely practicable, unless the cyst has a well-defined wall, and is therefore not applicable to traumatic cysts and other so-called pseudocysts. In several instances complete extirpation has been performed after the multilocular character of the cyst or the presence of papillary projections upon its inner surface has suggested the existence of an adenomatous growth. Complete removal of these proliferation cysts has been believed to offer the best chance of avoiding recurrence, although in several instances incision and drainage of cysts believed to belong to this type have been followed by recovery. A fatal result is due to gangrene of the intestine, hemorrhage, or peritonitis; when dense adhesions, the proximity of bloodvessels, or the deep situation of the tumor has prevented the completion of attempted extirpation, the mortality has been greater. When a cyst occupies the usual position between stomach and transverse colon, it is in most instances bound by adhesions to adjacent structures, and removal is difficult; when, however, the cyst lies within the mesocolon, adhesions are usually less abundant, and a considerable proportion of cysts which have been extirpated have had this situation. The operation is least difficult when the cyst occupies the tail of the gland, which serves as a pedicle and allows the tumor to be drawn into the wound; it is more difficult the nearer the cyst approaches the duodenum.

When cysts have been partially removed the wound has been drained and healing has occurred by granulation. In most instances of complete extirpation, pancreatic fistula has been avoided, but in two cases cited

by Körte pancreatic secretion discharged through the wound. Zweifel removed the entire pancreas save a part of the head 3 cm. in length; glycosuria was present ten days later, and persisted about twelve days, but at the end of two months had disappeared.

The disadvantages of incision and drainage are the occurrence of pancreatic fistula persisting for a considerable period, the possibility of hernia at the site of operation, and the occasional recurrence of the tumor. The resulting wound often heals slowly, and is complicated by the formation of a pancreatic fistula, from which there may be copious secretion; in the case of Cushing from 500 to 600 cc. of fluid were discharged during twenty-four hours. Pancreatic ferments may be demonstrable in the secretion from the wound immediately after operation, or may make their appearance several weeks later; unless care is exercised, there may be erosion of the skin about the wound. The cyst walls collapse, and by formation of granulations from the surrounding connective tissue the cavity is finally obliterated. This process cannot be completed when the cyst has an epithelial lining.

A fistula may persist a considerable time; in a case described by Murray a fistula was present during three years. The danger of injecting irritant substances into a fistulous tract is illustrated by a case described by Lazarus; death with collapse, due perhaps to hemorrhagic necrosis of the pancreas, followed the injection of silver nitrate. Infection of a fistulous tract may occur. In some instances there has been hemorrhage from a fistula; curetting of the tract is attended with danger, since dilated bloodvessels may be present in the wall. Closure of a pancreatic fistula has been hastened by making a second posterior opening, thus affording better drainage, or rarely by extirpation of the entire tract.

Healing of a pancreatic cyst is associated with the formation of scar tissue in the pancreas, and chronic inflammation resulting from the presence of the cyst may persist. In four cases in which recovery has followed operation diabetes mellitus has resulted.

### CARCINOMA OF THE PANCREAS

**Incidence.**—In the statistics of Bashford malignant growth was primary in the pancreas in males in 526 among 33,788 instances of cancer, and in females in 474 among 50,660 cases. In the statistics of Segré, among 11,472 autopsies, there was carcinoma of the pancreas in 127 and sarcoma in 2 instances. Among 106 reported cases of primary cancer collected by Mirallié<sup>1</sup> in 1893, 69 were in men and 37 in women, the disease being almost twice as frequent in men as in women. Cancer of the pancreas like that of other organs usually occurs during middle life, although there have been instances of its appearance at a very early age. Kuhn has described carcinoma of the pancreas in a child two years old, and Simon found the same disease in a boy thirteen years of age.

**Secondary Carcinoma.**—Since the pancreas is surrounded by organs which may be the seat of primary new growth, it is often difficult, when

<sup>1</sup> *Gaz. des Hôpitaux*, 1893, lxvi, 889.



the tumor has attained considerable size, to determine whether it is primary in the pancreas or has invaded it from without. Metastatic tumors occasionally occur in the pancreas, but the organ is more frequently the seat of secondary invasion by cancer of the stomach, duodenum, biliary passages, or other organs. Since the pyloric region and the posterior wall of the stomach are the most frequent situations of gastric cancer, secondary involvement of the head of the pancreas readily occurs and is followed by chronic interstitial inflammation of the body and tail as the result of compression of the duct of Wirsung. Olivier has described adenocarcinoma occupying the head of the pancreas, apparently originating from Brunner's glands of the duodenum.

**Pathology.**—Carcinoma of the pancreas is much more common in the head than in other parts of the gland. Among 57 cases collected by Segré, the tumor in 19 instances occupied the whole gland, in 35 the head, in 2 the body, and in 1 the tail. In the cases of primary cancer collected by Marallié the head of the pancreas was affected in 82 of 113 cases. Hansemann has described a type of pancreatic cancer which affects diffusely the whole gland. In most cases alveoli of cancer cells are embedded in abundant, dense, fibrous stroma; the tumor is hard and of the scirrhus type. Less frequently the neoplasm is cellular and soft or encephaloid; several cases of colloid carcinoma have been described. A cystic epithelioma is described by Roux.

Since the pancreas contains several distinct structures—namely, glandular alveoli, ducts, and islands of Langerhan—the attempt has been made to determine the histogenesis of different types of new growth. In most instances epithelial neoplasms of the pancreas are adenocarcinoma. These tumors, according to Hulst, are probably derived from the ducts of the gland. Where the glandular type is absent and alveoli of the tumor are formed by irregular polygonal cells closely packed together, Hulst<sup>1</sup> thinks it more probable that the tumor has its origin in the secreting alveoli. Nevertheless, in a case carefully studied by Olivier a tumor of the tail of the gland which in part exhibited the last-named type could be traced to the ducts with which alveoli of cancer cells were in places continuous. Fabozzi, from a study of 5 cases of this kind, designated by him *carcinoma solidum*, reaches the conclusion that such tumors are derived from the islands of Langerhans, but Hulst, on the contrary, found no relation between the islands of Langerhans and the alveoli of tumor cells. Ssobolew has suggested the possibility that a cancer derived from the islands of Langerhans might exert upon carbohydrate metabolism that influence which is attributable to the normal gland, and might prevent the occurrence of diabetes even though the entire gland were destroyed.

**Adenoma.**—Adenoma, unassociated with cyst formation, occurs rarely, and in most instances found at autopsy has given no discomfort during life. An exception is the encapsulated tumor of the head of the pancreas described as fibro-adenoma by Biondi; it was palpable and caused slight jaundice. Nicholls described a tawny yellow tumor which

<sup>1</sup> *Virchows Archiv*, 1905, clxxx, 228.

was the size of a large pea and had the structure of the island of Langerhans; a similar tumor is described by Helmholtz.

**Sarcoma.**—Sarcoma of the pancreas occurs with far less frequency than carcinoma. Kakels,<sup>1</sup> in 1902, collected 21 instances, among which only 10 were certainly primary in the gland; in 3 of the latter the tumor occupied the tail of the pancreas. Lymphosarcoma, angiosarcoma, fibrosarcoma, and medullary sarcoma have been described. The age of those affected has varied from four to seventy-four years.

**Pathology of Complications.**—Since *diabetes mellitus* not infrequently occurs with carcinoma, and is due to complete or partial destruction of the organ, the changes in the gland caused by the new growth are of considerable importance. Compression of the duct of Wirsung caused by the tumor mass, which is usually situated in the head of the gland, is followed by chronic interlobular inflammation of that part of the gland from which the outflow of secretion is hindered. The secreting parenchyma is destroyed, while the islands of Langerhans tend to persist in the newly formed fibrous tissue. Pearce<sup>2</sup> has studied the changes caused by the presence of carcinoma. At the edge of the advancing cancer the secreting parenchyma is invaded and replaced by new growth and newly formed connective tissue, but the islands of Langerhans persist in the stroma, and occasionally are uninvaded, even though enclosed by a mass of tumor cells; much hypertrophied islands are found. Carcinoma with permanent glycosuria was present in only one case studied by Pearce, and was associated with advanced chronic inflammation, implicating the islands of Langerhans.

As the tumor increases in size, adhesions may bind it to the stomach, duodenum, and adjacent organs, and symptoms are frequently caused by *pressure of the enlarging mass*. The following possibilities are named by Friedreich, who cites cases in illustration of each. There may be closure of the duodenum or the pylorus, with consequent dilatation of the stomach; occasionally the cardiac end of the stomach is compressed. In one case the stomach was compressed against the anterior abdominal wall. Compression of the transverse colon may cause symptoms of intestinal obstruction. Carcinoma affecting the tail of the pancreas has compressed the left ureter, causing hydronephrosis. Compression of the common bile duct causes jaundice. The growth may compress the superior mesenteric artery and vein, or the splenic artery and vein; pressure upon the portal vein causes ascites, while pressure upon the inferior vena cava causes oedema of the lower extremities. Pulsation of the aorta may be transmitted to the abdominal wall. Necrosis and ulceration may occur in tumor tissue which has invaded adjacent organs, and ulceration of the stomach or of the duodenum may cause the symptoms which are usually associated with primary cancer of these organs.

**Symptoms.**—When the tumor occupies the head of the gland, *jaundice* is usually present, and, being due to progressive compression of the duct, never recedes, but gradually increases in intensity until finally it merits the designation "black jaundice;" the gall-bladder is distended and is

<sup>1</sup> *Amer. Jour. Med. Sc.*, 1902, cxxiii, 471.

<sup>2</sup> *Ibid.*, 1904, cxxviii, 478.

palpable in the usual situation. In 23 of 35 cases of carcinoma of the pancreas described by Heiberg<sup>1</sup> the tumor was limited to the head of the pancreas and in 19 of these cases jaundice was present; in two instances there were no symptoms of pancreatic disease. Cancer of the body or tail of the gland may be unaccompanied by jaundice and other symptoms referable to compression of the biliary passages.

*Pain* is one of the earliest and most constant symptoms, and is usually seated in the epigastric region radiating toward the back, shoulders, or sternum; the right hypochondrium may be the seat of greatest pain when the tumor is situated in the head of the gland. The character and severity of the pain vary considerably; it may continuously increase in intensity until death, and may be of the intense severity which has been referred by many writers to pressure upon the cœliac ganglion and its branches. Intermittent colicky pain has been regarded as true pancreatic colic due to obstruction to the outflow of the pancreatic secretion caused by compression of the pancreatic duct. Similar pain may be the result of compression of the bile passages.

A *tumor mass* has been palpable in a relatively small proportion of the reported cases. Mirallié found that the tumor was palpable in from one-fourth to one-fifth of 113 cases which he collected. In the statistics of Ancelet, from which secondary tumors of the pancreas were not excluded, a tumor was present in 36 in the epigastrium, in 4 in the right, and in 2 in the left hypogastrium, while in 4 its situation was not accurately designated. The tumor must be of considerable size to be felt, especially when the abdominal wall contains abundant fat or is muscular; extreme tenderness may interfere with palpation. Although the tumor is usually immovable, it may descend with inspiration, and occasionally transmits pulsation from the aorta. In some cases the distended gall-bladder has been mistaken for a tumor mass, while at times both tumor and enlarged gall-bladder have been distinguishable.

Symptoms referable to the *gastro-intestinal tract* not infrequently precede more definite evidence of pancreatic carcinoma. There may be lack of appetite or actual distaste for food, especially, it has been thought, for meat. There may be discomfort after eating, eructations, nausea, or vomiting. Compression of the pylorus or of the duodenum may cause dilatation of the stomach, and in some instances symptoms referable to this condition have been the only evidence of the disease (Pilliet). The vomitus in such cases may contain blood. Constipation has been found much more often than diarrhœa, while constipation and diarrhœa may alternate; the stools may be normal.

Disturbance of digestion referable to lack of pancreatic juice in the intestine has been noted more frequently with carcinoma than with other diseases of the gland; nevertheless, Mirallié found only 9 cases with *fatty stools* among 113 instances of pancreatic carcinoma. Oser has collected 8 and Fitz 3 additional cases from the literature of the subject. Fitz found only 2 cases in which cancer of the pancreas was accompanied by disturbed digestion of proteins manifested by the

<sup>1</sup> *Zeit. f. klin. Med.*, 1911, lxxii, Heft 5.



presence of numerous undigested muscle fibres in the feces. Bulky stools are believed by Oser to be a symptom of pancreatic disease, and occur as the result of imperfect digestion of fats, proteins, and carbohydrates.

Since carcinoma of the pancreas in a large proportion of the cases invades the head of the gland, *jaundice* due to compression of the common bile duct is a frequent symptom, occurring in three-fourths of the cases, and, since the lesion in a large proportion of the cases has its origin in this part of the gland, frequently occurs as one of the earliest symptoms. Moreover, carcinoma of the pancreas, save for cholelithiasis, is the most frequent cause of occlusion of the common bile duct, and has been the cause of obstruction in 54 of 139 cases of non-calculous occlusion cited by Ecklin.<sup>1</sup> Jaundice due to compression of the duct may appear suddenly, and, once established, exhibits no remission, but steadily increases in intensity. When its sudden appearance is accompanied by colicky pain, cholelithiasis is closely simulated.

The condition of the *gall-bladder* and of the liver with obstruction of the common bile duct by cancer of the pancreas has been much discussed. From a study of a considerable number of cases of obstruction of the common bile duct due to a variety of causes, Courvoisier found that with obstruction due to biliary calculi the gall-bladder is usually contracted, while with occlusion due to other causes the gall-bladder is usually dilated. The statistics collected by Ecklin confirm this view. Among 172 instances of obstruction of the common bile duct due to gall-stones, the gall-bladder was contracted in 110, normal in 34, and dilated in 28 cases. On the other hand, among 139 instances in which the common bile duct was obstructed by other causes, the gall-bladder was contracted in only 9, normal in 9, and dilated in 121 cases; among 62 of these cases constriction of the common bile duct was due to carcinoma of the pancreas, and the gall-bladder was dilated in 58 instances. Contraction of the gall-bladder with biliary calculi is the result of inflammatory changes, whereas, with obstruction due to carcinoma of the pancreas or other cause, inflammation is usually absent and the gall-bladder is dilated.

Bard and Pic attached much importance to absence of enlargement of the *liver* with carcinoma of the pancreas. Mirallié, nevertheless, found the liver enlarged in 17 cases. Oser cites the cases of Friedreich and of Kellermann, in which the liver contained, during the terminal stage of the disease, secondary nodules as large as an apple, and maintains that the liver with cancer of the pancreas has no constant character.

Compression of the portal vein may cause *ascites* and other evidences of portal obstruction, such as swelling of the spleen and hemorrhoids. In 13 of 113 cases of primary carcinoma collected by Mirallié, ascites was present. Cases with chylous ascites presumably due to rupture of the thoracic duct have been described.

*Glycosuria* and other symptoms of *diabetes mellitus* not infrequently accompany cancer of the pancreas; among 50 cases Mirallié has found glycosuria in 13, and Oser subsequently collected 8 additional instances

<sup>1</sup> *Inaug. Diss.*, Basel, 1896.

of persistent glycosuria and 2 of alimentary glycosuria. Diabetes was present in 2 cases described by Pearce, and alimentary glycosuria in 1. Cancer of the pancreas is an infrequent cause of diabetes. Islands of Langerhans persist within the stroma of the new growth and prevent glycosuria until destruction of the pancreas is far advanced. The glycosuria of pancreatic cancer disappears before death.

The *cachexia* usually associated with malignant growth is said to proceed with special rapidity when the pancreas is the seat of the disease. Partial exclusion of pancreatic juice from the intestine and obstruction to the outflow of bile doubtless contribute to cause weakness and emaciation. Kellermann, who has described a case of cancer of the pancreas unaccompanied by cachexia, has been able to find only three similar cases in the literature of the subject.

The *temperature* with carcinoma of the pancreas is normal or subnormal unless there are complications accompanied by infection.

**Diagnosis.**—The features of greatest importance are jaundice increasing gradually, attaining great intensity, and associated with dilatation of the gall-bladder, the presence of a tumor in the epigastric region, rapid emaciation, and advanced age. In the absence of both tumor and jaundice diagnosis is hardly possible. Symptoms indicative of impaired pancreatic function are present in a relatively small proportion, but give definite evidence that the disease is located in the gland.

When jaundice is present, differential diagnosis between *cholelithiasis* and carcinoma is important. In certain cases of pancreatic carcinoma biliary symptoms serve to distinguish the two lesions. Jaundice usually appears gradually with carcinoma and increases without remissions, while with biliary colic the onset is more sudden and the progress more interrupted. Impacted calculi may, however, cause progressively increasing jaundice of great intensity; the gall-bladder is dilated in only a sixth of the cases, but with carcinoma of the pancreas, on the contrary, the gall-bladder is dilated with few exceptions. A palpably enlarged gall-bladder, therefore, gives evidence that cholelithiasis is not present, but the absence of this symptom is not equally significant, since the dilated organ is not always palpable, particularly when the abdominal wall contains abundant fat. Rapid emaciation and intense epigastric pain point to cancer of the pancreas. With carcinoma the temperature is usually normal or subnormal, but with cholelithiasis fever is not infrequently present.

Jaundice caused by *carcinoma of the liver, bile passages, duodenum, or stomach, compressing the common bile duct*, has the gradual onset and progressive character already mentioned, but emaciation and weakness are said to occur less rapidly than with carcinoma of the pancreas. Tumor has been recognized in a relatively small proportion of cases of cancer of the pancreas, but doubtless this proportion would be much increased by examination under anesthesia with the stomach and colon empty. A tumor mass having its origin in the head of the pancreas is deeply situated in the epigastric or umbilical region, and is usually defined with difficulty. The tumor is usually less movable than tumors of the pylorus or of the colon, and its position is unaffected by distension of these organs. Pulsation transmitted from the aorta is not expansile.

Both dilatation of the stomach and intestinal obstruction may be caused by carcinoma of the pancreas. The diagnosis between primary carcinoma of the pancreas and malignant growth arising from the common bile duct or duodenum is scarcely possible.

Tumor mass due to *carcinoma of the tail of the pancreas* may be mistaken for cancer of the cardia or of the colon. Takayasu describes a case in which an apparently immovable tumor, the size of a hen's egg, was felt behind the left rectus muscle. With inflation of the stomach, which lay above it, the tumor partially disappeared, and with inflation of the colon, which was at its lower margin, disappeared completely. Operation confirmed the diagnosis of carcinoma of the pancreas.

**Treatment.**—Medical treatment is directed to alleviation of symptoms, such as pain, jaundice, digestive disturbances, and diabetes. The administration of an emulsion prepared from the fresh pancreas of a pig has been found to aid digestion of fats and of protein when obstruction of the pancreatic ducts prevents entrance of pancreatic juice into the intestine (Fles); for the same purpose commercial pancreatin, which contains both trypsin and steapsin, has been recommended.

In a small number of cases tumors of the pancreas have been removed by *operation*. In a considerable proportion of the cases the patient has survived the immediate effects of the operation. Of 13 cases collected by Körte and by Mayo Robson, 5 died as the immediate result of the operation, whereas 5 are known to have died within from a few weeks to five months after the operation. In one instance (Biondi) a tumor, palpable on the left side of the abdomen, was removed from the head and body of the pancreas, and was found to be a fibro-adenoma; one and a half years later the patient was well. It is noteworthy that among the tumors which have been removed those types which are found least frequently have been relatively common; sarcoma has occurred three times, and in six cases the growth arose from the tail of the gland, causing a palpable tumor on the left side of the abdomen. Franke<sup>1</sup> believed that he had removed the entire pancreas, but its complete absence was not confirmed by autopsy; sugar was found in the urine from the fifth to the nineteenth day after operation, and death occurred in five months.

For the *relief of complications* a variety of palliative operations have been performed, but it is doubtful that they have materially prolonged life or added to the comfort of the patient. When jaundice due to compression of the common bile duct has caused much discomfort, cholecystenterostomy has been performed. In several instances the patient has lived from six to eighteen months, and the condition apparently has been improved. Little improvement has followed the formation of an external biliary fistula, and death has usually occurred a short time after operation (Nimier). When persistent vomiting and dilatation of the stomach indicate compression of the pylorus or of the duodenum, gastro-enterostomy may give relief, but since the biliary and pancreatic ducts are usually compressed, the operation has not the advantages which it offers for the relief of the symptoms of pyloric carcinoma.

<sup>1</sup> *Verhandl. d. Deutschen. Gesell. f. Chir.*, xxx, Congress, 1901, 265.



## CHAPTER IX

### DISEASES OF THE PERITONEUM

BY HUMPHRY DAVY ROLLESTON, M.A., M.D. (CANTAB.), F.R.C.P.

**Introductory.**—The peritoneum is a serous sac of extensive dimensions. In fact, when all its reflections and fossæ are taken into account, its superficial area is but slightly less than that of the skin. In the female it differs from all other serous cavities in that its potential cavity opens indirectly externally through the Fallopian tubes, but in the male it is completely shut off from the exterior.

The peritoneum has remarkable powers of absorption. Thus in a dog or rabbit, fluid equal to 10 per cent. of the body weight of the animal can be absorbed from the peritoneal cavity in half an hour. Fluid and soluble substances are conveyed away by the bloodvessels, while, in addition, the lymphatics, with the aid of phagocytes, carry off insoluble bodies, including microorganisms. It was formerly thought that the peritoneal cavity was in direct communication with lymphatic vessels by open apertures or “stomata,” and that it was an appendage of the lymphatic system or an immense lymph space. Muscatello<sup>1</sup> and MacCallum,<sup>2</sup> however, have shown that the endothelial lining of the peritoneum is everywhere continuous and complete, and that there is no actual communication between its cavity and the lymphatics, through which its contents can be pumped by purely physical means, viz., the contractions of the diaphragm.

The peritoneum covering the under surface of the diaphragm differs from the rest of the peritoneum in having a number of depressions or pits, formerly described as stomata or lacunæ, opening into the lymphatic vessels, but in reality closed by a continuous layer of endothelial cells. These cells, however, by phagocytic action, play an important part in the absorption of solid particles, and Buxton<sup>3</sup> has shown that bacteria injected into the peritoneal cavity of animals are immediately absorbed by the lymphatics of the diaphragm and reach the general circulation in a few minutes. When the endothelial layer of the peritoneum is intact, microorganisms are probably not absorbed by the bloodvessels, but damage to these delicate cells allows rapid absorption of bacteria to take place, and hence septicemia may result. The preservation of the endothelial lining of the peritoneum is therefore of the greatest importance.

In health, secretion of fluid, mainly by the great omentum, into the peritoneal cavity and its absorption therefrom are so evenly balanced

<sup>1</sup> *Virchows Archiv*, 1895, cxlii, 327.

<sup>2</sup> *Johns Hopkins Hosp. Bull.*, 1903, xiv, 105.

<sup>3</sup> *Jour. Med. Research*, Boston, 1907, xvi, 25.

that there is just enough fluid to keep the serous surfaces moist and free from friction. In morbid conditions this state of equilibrium is disturbed and the amount of fluid may become excessive—ascites. The pathological effects produced by the drying of the peritoneum are not so well known. It has been shown experimentally that it diminishes the power of absorption, and in practice it is clear that it impairs the vitality of the peritoneum, since it readily splits or tears on handling. The small amount of fluid also plays an important part in the defense of the peritoneum against infection by exerting a bactericidal action.

The lymphatic trunks draining the peritoneal cavity run up into the thorax, especially to the anterior mediastinal glands (Durham<sup>1</sup>). The peritoneum covering the diaphragm and the omentum is particularly active in this process of absorption, removing not only inert bodies but microorganisms from the peritoneal cavity; the omentum is, further, a most important factor in preventing peritonitis, since it removes microorganisms from the abdominal cavity before they can exert their pathogenic effect locally. Thus, twenty-four to forty-eight hours after the injection of bacteria into the peritoneal cavity the omentum may have rendered the peritoneum perfectly sterile, although cultures from the omentum itself or from glands in the anterior mediastinum show the path by which absorption has been effected. The omentum is apt to attach itself to any inflamed organ or possible source of infection, and thus to localize the peritoneal infection. The absorptive powers of the peritoneum are diminished by the backward pressure of chronic venous engorgement, probably by lymphatic obstruction, and by less vigorous peristaltic and diaphragmatic movements.

The visceral peritoneum is quite insensitive to pain, while the parietal layer is extremely sensitive (Lennander, Franke<sup>2</sup>). Excessive peristalsis and dragging on the mesentery cause pain because traction is thus exerted on the parietal peritoneum which is supplied by the nerves of the abdominal wall. The deep tenderness on pressure in localized or universal peritonitis is due to inflammation involving the parietal layer, and tenderness in inflammatory conditions of the stomach, appendix, etc., depends on lymphangitis and extension of inflammation to the parietal peritoneum. The insensibility of the visceral peritoneum and abdominal viscera is seen in abdominal operations under cocaine. Further, when inflamed, the visceral peritoneum is as insensitive as in health (Lennander). But the cocaine may be partly or wholly responsible for the anesthesia (Kast and Meltzer, Franke).

*Comparison of the Peritoneum with Other Serous Membranes.*—Like the other serous membranes the peritoneum is extremely resistant to the spread of inflammation from the tissues of the body wall covering it. It, however, is often affected, together with the adjacent pleuræ and pericardium, and infection and inflammation readily spread through the diaphragm. This associated inflammation is spoken of as polyorrhomenitis, or multiple serositis, and may be acute or chronic, but is more often<sup>3</sup> localized or at least partially circumscribed than universal.

<sup>1</sup> *Jour. Path. and Bacteriol.*, Edinburgh and London, 1897, iv, 338.

<sup>2</sup> Franke, *Berlin. klin. Wchnschr.*, 1912, xlix.

In common with the other serous membranes the peritoneum suffers mainly from infections derived from the organs which it surrounds and protects. Thus, like the lungs and synovial membranes, it is often affected by tuberculosis, because that form of infection commonly attacks the intestines. While unlike the pericardium, it may be regarded as immune to acute rheumatic inflammation, which is not recognized as attacking any of the organs covered by the peritoneum, with the possible exception of the vermiform appendix. Like the other serous membranes, it may be infected by the blood-stream, but hematogenous infection of the peritoneum is subordinate in importance to the local origin of infection. In common with other serous membranes inflammation of the peritoneum has a great tendency to lead to adhesions.

**Immunity.**—The natural resistance of the peritoneum varies in individuals. Different parts of the peritoneal cavity probably differ in their power of resistance; the pelvic peritoneum is thicker in women than in men, and it is possible that this has some influence in its comparative immunity to infection. An attack of peritonitis leaves thickening of the affected area, and thus may to some extent account for the increased resistance to infection which a past attack confers.

The defensive powers of the peritoneum are further considered under the heads of Pathogeny (page 671) and Morbid Anatomy (page 675 of Acute Peritonitis).

### ASCITES

Ascites is the presence of free fluid in the peritoneal cavity, and is the counterpart of a pleural effusion. The name hydroperitoneum indicates that the fluid effusion is not manifestly due to inflammation. The presence of fluid in excessive amounts in the peritoneal cavity may depend on the passage of fluid in increased quantities into the sac, the rate of absorption failing to keep pace with this; or on interference with the normal process of absorption, the secretion of fluid into the cavity remaining normal or being increased. The passage of increased amounts of fluid into the peritoneal cavity mainly depends on changes in the endothelial cells of the peritoneum brought about by poisons; this process occurs in inflammation, and is then spoken of as an exudation. When the action of poisons cannot be assumed and the ascites appears to be the result of increased venous or lymphatic pressure—passive or mechanical effusion—the process is spoken of as a transudation. It is obvious that these two processes overlap; thus, passive venous engorgement, by interfering with the vitality of the endothelium, will produce changes analogous to those wrought by poisons.

**Etiology.**—The causes of ascites in the order of their importance are:

1. *Backward pressure* from tricuspid regurgitation may give rise to copious ascites. In 224 cases in which ascites to the extent of a quart or more was found after death, 89 (or 40 per cent.) were due to various forms of heart disease (Cabot<sup>1</sup>). Although in many of such instances chronic

<sup>1</sup> *Amer. Jour. Med. Sci.*, Phila., 1912, cxliii, 1.



peritonitis may be the determining cause of ascites, this is not always so. In some cases the brunt of the backward pressure seems to fall on the hepatic veins, with the result that there is ascites without œdema of the feet. This condition, which has been called hepatic asystole, may imitate cirrhosis of the liver. In some cases of adherent pericardium there is a high grade of nutmeg liver, ascites, and little chronic peritonitis. The adherent pericardium may be the result of rheumatic fever, or be tuberculous; in some cases the tuberculous nature is only revealed by microscopic examination. Pick<sup>1</sup> described pericarditic pseudocirrhosis, but doubt has been cast on its existence as a distinct morbid entity; it is advisable to keep an open mind on this difficult question, but probably some of the cases so described may be included under the heading either of advanced nutmeg liver or of chronic peritonitis associated with adherent pericardium. Acute cardiac failure gives rise to a small amount only of ascitic effusion, which in itself is of no clinical importance. Stricture of the hepatic veins, or thrombosis of the inferior vena cava occluding the orifices of the hepatic veins, may give rise to marked ascites.

2. *Chronic Peritonitis*.—(a) Simple, either universal or diffuse, which does not involve the whole of the peritoneum, but is more or less limited to part of the abdominal cavity, especially the upper half over the liver and spleen. (b) Associated with infection of the peritoneum by malignant disease. It may be associated with so-called "cirrhosis of the stomach," which is generally regarded as carcinomatous. (c) In rare instances innocent tumors, such as ovarian cystadenomas and fibromas, and uterine fibromyomas, set up sufficient chronic peritonitis to cause ascites. Papilloma of the ovaries may give rise to multiple implantation growths on the peritoneum, which irritate the peritoneum and so cause ascites. (d) Tuberculous peritonitis. Simple or "idiopathic" ascites, especially in young girls, is in many cases tuberculous.

3. *Cirrhosis of the Liver*.—Hypertrophic biliary or Hanot's cirrhosis, which is comparatively rare, is either not complicated by ascites or only at a very late stage, and then to a slight degree. In portal or common cirrhosis, ascites is met with in 80 per cent. of the cases fatal from the effects of the disease. It may be due to the cirrhosis alone, and is then a late or terminal phenomenon, and rarely requires tapping more than twice. Ascites may be merely associated with cirrhosis and be caused by chronic simple or tuberculous peritonitis, or by cardiac failure. In these cases numerous tapplings may be necessary.

4. *Other Morbid Conditions of the Liver*.—Hepatic syphilis is often associated with chronic perihepatitis and peritonitis; but as it cannot always be proved that the accompanying ascites is set up in this indirect manner, syphilis of the liver may be regarded as a cause of ascites. Out of 56 cases of hepatic syphilis, ascites occurred in 23, or 41 per cent. (T. McCrae<sup>2</sup>). A lardaceous liver in rare instances, and then usually in children, appears to be responsible for ascites. In malignant disease of the liver ascites is common; in most cases the growths project from

<sup>1</sup> *Ztschr. f. klin. Med.*, Berlin, 1896, xxix, 385.

<sup>2</sup> *Amer. Jour. Med. Sci.*, Phila., 1912, cxliv, 625.

the capsule and by irritating the peritoneum induce ascites; but growths may press upon or invade and block up large branches of the portal vein inside the liver, especially in primary carcinoma with cirrhosis. In some cases new growth may block up the capillaries in the liver so widely as to produce marked portal obstruction and ascites, as is well shown in secondary melanotic sarcoma of the organ (Hektoen and Herrick<sup>1</sup>). Ascites may occur in hepatic and abdominal lymphadenoma, and is explained in the same way as in malignant disease. From an analysis of 100 cases of ascites in Egypt, Phillips<sup>2</sup> finds that 30, and possibly 52 per cent., of these cases were due to the effects of chronic malaria in the liver and spleen.

Perihepatitis is considered under Simple Chronic Peritonitis.

5. *Thrombosis of the portal vein* is rare but usually causes a rapid and extensive ascitic effusion, which speedily recurs after tapping. Pressure on the portal vein may, but does not necessarily, produce ascites.

6. In universal *renal dropsy* the peritoneum may contain free fluid.

7. *Inflammation of the Peritoneum*.—Subacute and acute inflammation of the peritoneum will, of course, give rise to an effusion.

In addition, rupture of hydatid, ovarian, or other cysts may give rise to free fluid in the peritoneal cavity; in the case of ruptured hydatid cysts, absorption will, as a rule, rapidly lead to its removal. Rupture of lymphatic vessels or lacteals will cause a chylous effusion. Effusions of bile (choleperitoneum) and of pure blood (hemoperitoneum) are referred to elsewhere.

**Pathology.**—The *morbid anatomy* of ascites is, except for the mechanical effects due to abdominal distension, that of the underlying cause, such as chronic peritonitis, cirrhosis, and new growth. Portal obstruction when present increases the anastomotic channels between the systemic and the portal veins. The veins of the peritoneum, especially at the back of the abdomen, become manifestly enlarged; veins in any adhesions become prominent, and the parumbilical vein in the falciform ligament may reach a large size; the veins at the lower ends of the œsophagus and rectum also become tortuous and dilated. The abdominal muscles become stretched and atrophied; the diaphragm is pushed up, and may show hypertrophy from increased work. Upward displacement of the diaphragm may compress the lower lobes of the lungs. The presence of adhesions may produce encysted or loculated ascites.

The characters of ascitic fluid vary according to the causes at work. Thus, when there is inflammation of the peritoneum (exudates) the specific gravity and amount of contained protein are higher than in ascites associated with backward pressure (transudates). Serous ascitic fluid is clear, transparent, and greenish or faintly yellow in color. The reaction is alkaline, and the specific gravity under 1.012 in mechanical effusions, or hydroperitoneum, and 1.018 or higher in the exudations in subacute or chronic peritonitis. The amounts of solids and contained proteins vary. In simple effusions due to renal disease there may be only 0.3 per cent. or less of protein, while in inflammation the amount

<sup>1</sup> *Amer. Jour. Med. Sci.*, Phila., 1891, cxvi, 255.

<sup>2</sup> *Records of the Egyptian Government School of Medicine*, 1904, ii, 47.

may be 4 per cent. In some instances, especially of ascites associated with rupture of ovarian cystadenomas, the fluid is sticky from the presence of pseudomucin. Occasionally cholesterin, urea in traces or in larger amounts, and various extractives are present. After repeated tapplings the character of the effusion may alter, and from added inflammatory changes in the peritoneum be of higher specific gravity and show a higher percentage of proteins.

In jaundiced patients the ascitic fluid contains bile pigment. A blood-stained or hemorrhagic ascites may occur in (1) intra-abdominal malignant disease, from leakage; this is rare in carcinoma and is more often associated with vascular or hemorrhagic sarcomas or endotheliomas. (2) Some cases of hepatic cirrhosis; here it is usually the result of trauma, such as rupture of a dilated vein in the peritonum or in vascular adhesions, either from traction or from direct injury by the trocar. As a rule, the blood-stained character of the effusion is seen not at the first but at a subsequent tapping. (3) Ascites is blood-stained in about one-fourth of the cases associated with ovarian cysts, and in about one-sixth of the cases of ascites associated with uterine fibromyomas (Cabot<sup>1</sup>). (4) Red-blood corpuscles have been found exceptionally on microscopic examination of the ascitic fluid in tuberculous peritonitis (Grenet and Vitry<sup>2</sup>). (5) A certain amount of blood-stained fluid, but rarely sufficient to be recognized clinically, may be associated with strangulated hernia, volvulus, infarction of the intestines, and hemorrhagic pancreatitis. Sometimes the ascitic fluid clots spontaneously on standing.

The *cells* seen on microscopic examination vary in the different kinds of ascites. As in the cytodagnosis of pleural effusions, a preponderance of any one form of cell is correlated with a special causal factor. Thus in ascites due to mechanical causes, *e. g.*, heart disease and hepatic cirrhosis, endothelial cells are those found; in tuberculous peritonitis small lymphocytes are present in a high percentage; and in other infections the predominant form of cell is the polymorphonuclear leukocyte. (For the cytology of ascites associated with new growth see p. 666.)

**Bacteriology.**—Ascitic fluid, at any rate, at the first tapping is usually sterile; as a result of paracentesis infection may occur. The colon bacillus and the tubercle bacillus are sometimes present. Jousset,<sup>3</sup> by the method of inocopy which consists in examining the clot produced spontaneously or by the addition of salted plasma, has proved that the tubercle bacillus is present in many cases of ascites in which a tuberculous origin was not suspected.

**Chylous, Chyliform, and Milky Non-fatty Ascites.**—These three forms are alike in their naked-eye resemblance to milk.

1. *Chylous ascites* is due to the escape of chyle from the lymphatics or receptaculum chyli. Wallis and Schölberg<sup>4</sup> collected 102 cases in 1910. The fluid is yellowish white, tends to accumulate very rapidly, and

<sup>1</sup> *Amer. Jour. Med. Sci.*, Phila., 1912, cxliii, 1.

<sup>2</sup> *Compt. rend. Soc. biol.*, Paris, 1903, lv, 959.

<sup>3</sup> *Arch. de méd. expér. et d'anal. path.*, Paris, 1903, xv, 289.

<sup>4</sup> *Quart. Jour. Med.*, Oxford, 1910-11, iv, 15.



its opalescence is constant at successive tapplings. The specific gravity is usually about 1.015. The fluid resists putrefaction and does not clot on standing, thus differing from chylous urine. It, however, separates into layers on standing, the fat accumulating on the surface. The distinctive odor of some special article of diet such as butter may be perceptible in it (Straus' sign). The amount of solids is about 4 to 6 per cent.; the percentages of fat and of protein vary considerably, and may be modified by changes in the diet; there is from 0.4 to 4 per cent. of fat in a very fine state of division; the amount of protein is usually about 3 per cent. Cholesterin is always present, but lecithin occurs only in traces. The reaction is alkaline or occasionally neutral. It accumulates very rapidly. The important characters of true chylous ascites are (1) the finely divided fat, and (2) the absence of leukocytes and other cells showing fatty change.

Chylous ascites is caused by obstruction of the thoracic duct or lymphatic vessels. Pressure from without by tumors or dense adhesions may obstruct the thoracic duct and lead to rupture of the receptaculum chyli or to leakage from its tributaries. Thrombosis inside and infiltration of the walls of the thoracic duct or receptaculum chyli with new growth, or even with tuberculosis, have also been responsible for chylous ascites. Malignant disease, by compressing the lacteals, may so raise the pressure that rupture occurs. Traumatic rupture and rupture attributed to whooping-cough (Wilhelm), to vomiting, and to muscular exertion have been recorded. Chylous ascites may be due to rupture of a chylous mesenteric cyst. It has been met with in only a few cases of filariasis. It should be explained that the free lymphatic anastomosis often obviates chylous ascites when from obstruction due to tumors and other factors it might be expected. A chylous peritoneal effusion may be accompanied by a similar condition in one or both of the pleuræ.

2. *Chyliform or fatty* differs from true chylous ascites in (a) that it is due not to leakage of chyle but to the formation of fat in the peritoneal effusion; (b) that the globules of fat are large, and (c) that cells containing fat are present in the fluid. The opalescence is not, however, always due to suspended fat, for in some instances it persists after all the fat has been removed; there is then a mixture of the two forms of adipose and milky non-fatty ascites. For this reason Wallis and Schölberg group these two forms together as pseudochylous. Chyliform ascites is usually associated with intra-abdominal new growth or with chronic peritonitis, tuberculous or simple. The fat may be derived from the cells of the new growth, or a poison generated in the growth may lead to the production of fat in the leukocytes and other cells suspended in the ascitic fluid. In chronic peritonitis the fat is thought to be formed in the cells in the exudation. In some instances fat in the ascitic fluid may depend on lipemia, which in its turn may be the result of milk diet. It has been suggested that a lipemic ascitic effusion may depend on disease of the pancreas (Gaultier<sup>1</sup>). It is much more common than true chylous ascites.

<sup>1</sup> *Compt. rend. et mém. Soc. biol.*, Paris, 1906, lxi, 429.

3. *Lactescent, Milky, Non-fatty Ascites*.—In some cases the milky opacity is due not to fat, as it is either absent or present in quantities insufficient to account for the milkiness, but to some other body such as a protein resembling casein, mucinoid bodies, or lecithin. Although resembling chylous and chyloform ascitic fluid to the naked eye in most respects, it does not separate into layers on standing. This form of ascites may occur in intra-abdominal malignant disease and in other conditions. In some instances only the later tapplings may show this condition, the earlier ones being clear; or later tapplings may be more milky than the first. In such cases it would appear to be in some way related to a low form of chronic peritonitis.

**Physical Signs**.—The abdomen is enlarged, especially in chronic ascites in which the abdominal muscles have become stretched and atrophied. Measurements of fifty inches are sometimes seen. An extreme grade of abdominal distension was recorded in a woman who has been very frequently tapped and measured eleven feet around the abdomen, which contained forty-seven and a half gallons of fluid after death (Duncan<sup>1</sup>). The abdominal distension is not exclusively due to fluid, but may vary from day to day from flatulency; considerable flatulent distension often precedes the discovery of recognizable ascites. Fetal ascites may be so extreme as to obstruct the birth of the child; the abdomen of a fetus has contained nine pints of fluid (Luker<sup>2</sup>).

In recent and acute ascites the distension is mainly anteroposterior, the abdomen being prominent, especially above the umbilicus, tense, and hard. This is probably due to contraction of the abdominal muscles which are irritated by the distension. In ascites of some duration the muscles become atrophied, flaccid, and thus separation of the recti abdominales and bulging in the flanks result. When, however, ascites comes on in a patient whose abdominal walls are already thin and weak, as in women after repeated pregnancies, the abdomen bulges in the flanks from the outset. The distension is, generally speaking, uniform. But in encysted ascites there is a more or less localized prominence which does not alter in position on movement. There is a positive intra-abdominal pressure (6 to 30 mm. Hg.) in ascites, which diminishes during paracentesis (Pitres,<sup>3</sup> Quirin<sup>4</sup>).

The skin is tightly stretched and may be shiny and present distended veins; in portal obstruction, as in cirrhosis, the large veins are chiefly above and around the umbilicus and in the line of the falciform ligament; but when the obstruction is in the inferior vena cava the veins running from the middle of Poupart's ligament to the costal arch are prominent, and, when considerably enlarged and tortuous, produce the condition spoken of as a "caput Medusæ." This venous dilatation is sometimes due to the pressure of enlarged glands, as in tuberculous or malignant peritonitis, but, as a rule, it is due to the pressure exerted by the ascitic fluid on the inferior vena cava, and therefore disappears after tapping.

<sup>1</sup> *Brit. Med. Jour.*, 1906, i, 1157.

<sup>2</sup> *Lancet*, Lond., 1913, i, 1309.

<sup>3</sup> *Compt. rend. Soc. biol.*, Paris, 1899, li, 674.

<sup>4</sup> *Deut. Arch. f. klin. Med.*, 1901, lxxi, 79.

In cirrhosis both sets of veins may be present, and after paracentesis the "caval" veins disappear while the portal veins persist (Gilbert and Villaret<sup>1</sup>). The caval veins are most prominent in the lower and lateral part of the abdomen. Occasionally a bruit is audible over these dilated veins in the epigastrium. The umbilicus becomes flush with the surface, after a time everted and tense, appearing as a thin-walled bulla, and has been known to burst when tapping has been unduly delayed. Any existing hernial sacs become distended with fluid. From stretching, the deeper layers of the skin rupture, and in a recent state reddish lines are seen, especially when the abdominal wall is lax after tapping; subsequently these lines appear as crinkled cicatrices, the well-known "lineæ albicantes." They are seen in the lower half of the abdomen. Edema of the abdominal walls may accompany and obscure the signs of ascites. The costal margins are expanded, and the abdomen moves little on respiration.

On palpation the resistance is fairly uniform. The characteristic thrill is readily brought out by flicking the surface in one flank. When the hand is placed flat on the abdomen and the tips of the fingers are sharply flexed, fluid between the abdominal wall and the liver or spleen, if enlarged, or an abdominal tumor, may be displaced and the firm surface of the previously obscured organ is distinctly felt; this is spoken of as "dipping."

Percussion brings out a dull note over the fluid, which collects first in the pelvis and then passes upward into the loins and hypogastric region, producing a horseshoe-shaped area of dulness. The umbilical and epigastric regions remain resonant except in those cases of chronic peritonitis in which, from shortening of the mesentery, the intestines cannot reach the front of the abdomen. The characteristic horseshoe-shaped distribution of dulness is sometimes disturbed by flatulent distension of the large intestine, especially in the right iliac fossa; while, conversely, dulness in the flanks may be due to liquid feces and not to free fluid in the peritoneum. Light percussion gives a duller note than more forcible percussion, as pressure displaces a layer of fluid between the abdominal wall and an adjacent coil of distended intestine. A very important sign of free fluid in the abdominal cavity is shifting dulness. The presence of adhesions may interfere with this test, and for its success some of the intestines must contain gas. In cases in which the amount of fluid is not sufficient to give this sign the patient may be put in the knee-elbow position and the anterior surface of the abdomen then percussed in the most dependent position for an impaired note.

**Results.**—Distension of the abdomen gives rise to fulness, weight, and pain in the tense parietes; "pain is a very common symptom in ascites, but is seldom or never described in accounts of that condition" (Gee<sup>2</sup>). The abdominal viscera are embarrassed, so that dyspepsia and constipation are common, the latter being partly due to the flabby

<sup>1</sup> *Rev. de méd.*, Paris, 1907, xxvii, 334.

<sup>2</sup> *Clinical Aphorisms from Dr. Gee's Wards, St. Bartholomew's Hospital Reports*, 1896, xxxii, 44. Aphorism No. 128.



condition of the stretched abdominal muscles. The uterus may be displaced and fluctuation can be detected by the finger on pelvic examination. The abdominal muscles atrophy, and the recti separate so that a hernial protrusion may occur. Pressure on the inferior vena cava may induce œdema of the legs, while compression of the renal veins leads to chronic venous engorgement of the kidneys and scanty high-colored urine of increased specific gravity with sometimes a trace of albumin—resembling that of a failing heart. Albuminuria may, of course, be due to renal disease which is often associated with chronic peritonitis. The upward displacement of the diaphragm pushes the heart up, so that the apex beat may be in the third interspace; in some cases there is a soft, systolic apex murmur, which may disappear when the abdominal distension is relieved. The breathing may be embarrassed and cyanosis appear, the underlying condition being collapse and œdema of the lower lobes of the lungs. In rare cases the pulmonary engorgement is so extreme that there is hemoptysis. The percussion note at the bases of the lungs behind is impaired.

**Diagnosis.—Differential Diagnosis.**—The physical signs of free fluid in the abdominal cavity may, to a certain extent, be reproduced by large cysts occupying almost the whole of the abdominal cavity. In women confusion sometimes arises between a large ovarian or par-ovarian cyst and ascites. An ovarian cyst may, as shown by the history, have been first noticed in one position and subsequently spread upward into the abdomen; the maximum abdominal girth is below instead of above the umbilicus; the umbilicus may be displaced toward the thorax or to one side of the middle line, dulness is present in the middle line and not in the flanks, and there is little constitutional disturbance, the ill effects being almost entirely mechanical. Ovarian cysts, however, may be accompanied by ascites set up by chronic inflammation of the peritoneum covering them, or they may rupture. In rare instances a huge hepatic abscess, hydatid cyst, pancreatic cyst, or hydronephrosis has been regarded as ascites; but in these cases there may be a history of localization of the cyst at an earlier period, and even at a later stage the abdomen is hardly ever so fully occupied as to present all the physical signs of ascites. In encysted peritonitis the physical signs are those of a large cyst, and the dulness does not shift as it does in ascites.

Among solid or semisolid tumors the rare but remarkable fatty tumors may very closely simulate ascites and their true nature be only suspected after repeated fruitless tapplings (see page 733).

Diffuse colloid carcinoma is rare, but, unless complicated by ascites, thrill and fluctuation are absent. In exceptional instances a distended urinary bladder, or even gall-bladder, has been regarded as ascites. As the patient should always pass water, or, if he cannot, be catheterized before the abdomen is tapped, the possible error of regarding a greatly dilated urinary bladder as ascites would be corrected. A greatly dilated stomach and a pregnant uterus with hydramnios have also been thought to be ascitic effusions. The absence of the concomitant signs of pregnancy should prevent ascites from being regarded as that condition; but a case of a uterine fibroid combined with ascites has been regarded as

pregnancy (Montgomery<sup>1</sup>). Great obesity with abdominal distension may imitate ascites, and in such cases it may be very difficult to exclude the presence of, at any rate, some free fluid in the abdomen. The distension due to tympanites should not be mistaken for ascites, since the abdomen is everywhere resonant, but when the abdominal parietes are laden with fat the percussion note may thereby be much impaired. Occasionally in adults with chronic intestinal obstruction distension of the intestines with fluid may simulate ascites, and in children with chronic enteritis this condition of pseudo-ascites has led to laparotomy. In such cases succussion due to the presence of gas as well as fluid feces in the intestines can often be obtained. Conversely, the writer has seen a case of ascites with constipation and vomiting due to gastritis regarded as intestinal obstruction.

**The Diagnosis of the Cause of Ascites.**—Jaundice points to malignant disease or cirrhosis of the liver, being deep in malignant disease and comparatively slight in cirrhosis. Recurrent ascites usually indicates simple chronic peritonitis. The evidence of a growth elsewhere makes the diagnosis of malignant disease almost certain. Heart disease or tuberculosis elsewhere renders backward pressure or tuberculous peritonitis probable. A history or evidence of alcoholism points to cirrhosis. Thrombosis of the portal vein, which is often a complication of cirrhosis, can hardly be diagnosed, but melena and rapid onset of ascites may suggest it. A history or the manifestations of syphilis point to this form of liver affection; the Wassermann reaction may be more marked in the ascitic fluid than in the blood (Esmein and Parvu<sup>2</sup>).

Enlargement of the liver, if quite smooth, may point to lardaceous change; if rough, to cirrhosis; and if extreme or definitely nodular, to malignant disease. Less marked enlargement and irregularity may suggest syphilis of the liver, a conclusion which would be strengthened by other evidence of syphilis, and may be clinched by recovery under antisiphilitic treatment. If ascites be associated with general oedema and albuminuria, renal disease is the probable cause. Multiple palpable tumors in the abdomen point to malignant disease, or in a less degree to tuberculous peritonitis. Fever and concomitant pleurisy are in favor of tuberculosis, as are scars in the neck. But enlarged glands above the left clavicle point to malignant disease.

By laparoscopy or inspection of the peritoneal cavity by means of a fine cystoscope introduced through a trocar after the ascites has been evacuated and air introduced, Jacobæus<sup>3</sup> has been able to recognize the cause of the ascites.

Age has some bearing on the diagnosis. Ascites in stillborn children is generally due to inherited syphilis. Tuberculous peritonitis is the commonest cause of ascites in children and young women, and cirrhosis, simple chronic peritonitis, and malignant disease in adults over forty years of age. Examination of the fluid drawn off may be of practical value. If blood-stained at the first tapping, malignant disease should

<sup>1</sup> *American Gynecology*, 1902, i, 449.

<sup>2</sup> *Compt. rend. Soc. biol.*, Paris., 1909, lxii, 159.

<sup>3</sup> *Trans. XVII Internat. Congress*, 1913, London (Sect. Med.).

be suspected; microscopic examination may show pieces of malignant growth or fragments of ovarian papilloma. In malignant disease multinuclear endothelial cells and a large number of cells showing atypical mitoses may be found, but in many instances the ascites is mechanical and due to pressure exerted by the growth, and shows a predominance of endothelial cells, the condition found in passive effusions, as in heart disease or cirrhosis. In other cases, again, there may be a considerable number of polymorphonuclear leukocytes, probably as the result of subacute inflammation; hence a diagnosis of malignant disease cannot always be made from examination of the cells in the effusion alone. Tenacious fluid may be due to rupture of an ovarian cystadenoma, and microscopic examination of the cells may confirm this.

Turbid fluid of a high specific gravity (1.020) points to inflammation. If the predominating cells are polymorphonuclear leukocytes there is subacute inflammation; but if the cells are mainly lymphocytes, tuberculous infection should be suspected and guinea-pigs should be inoculated with the fluid. It should be remembered that many cases of clear ascites are tuberculous in origin. The detection of tubercle bacilli in the feces has established the diagnosis in doubtful cases of ascites (Rosenberger<sup>1</sup>).

In hepatic cirrhosis the fluid is clear and shows a preponderance of endothelial cells (Cade,<sup>2</sup> Ross,<sup>3</sup> Gilbert and Villaret<sup>4</sup>). If complicated by infection, as may occur after tapping, there may be a large number of polymorphonuclear leukocytes. When tuberculous peritonitis supervenes the number of small lymphocytes will increase, but the lymphocyte count may be high in uncomplicated cirrhosis (Cabot<sup>5</sup>). The main diagnostic importance of a high percentage of endothelial cells is that it excludes acute or subacute infections and tuberculosis. If the opsonic index for tubercle bacilli be low in the ascitic fluid as compared with that of the blood serum, and if the opsonic index of the blood serum rises markedly after abdominal massage, tuberculous peritonitis is indicated. The tuberculin tests can also be employed.

**Prognosis.**—This depends in the first place on the cause. Thus, ascites in malignant disease leaves no room for hope of recovery, while that of tuberculous peritonitis is often followed by permanent cure. The ascites that recurs again and again in cases with secondary ovarian papillomas implanted on the peritoneum or in some cases of solid ovarian growths (Osler<sup>6</sup>) may be cured by removal of the primary growth.

When ascites supervenes in an emaciated subject of hepatic cirrhosis, the prognosis is bad, and tapping is not likely to be required more than twice before death closes the scene. The association of jaundice with ascites is rare except in malignant disease and hepatic cirrhosis, and is therefore a bad prognostic. In simple chronic peritonitis paracentesis may be necessary for a prolonged period; Rumpf's<sup>7</sup> patient was tapped

<sup>1</sup> *Amer. Jour. Med. Sci.*, 1907, cxxxiv, 830.

<sup>2</sup> *Arch. de méd. expér. et d'anal. path.*, Paris, 1906, xviii, 769.

<sup>3</sup> *Transactions of the Pathological Society of London*, 1906, lvii, 361.

<sup>4</sup> *Compt. rend. Soc. biol.*, Paris, 1906, lx, 820.

<sup>5</sup> *Jour. Amer. Med. Assoc.*, Chicago, 1912, lix, 2295.

<sup>6</sup> *Lancet*, 1907, i, 1409.

<sup>7</sup> *Deut. Arch. f. klin. Med.*, Leipsic, 1895, lv, 272. (Festschrift zu F. A. von Zenker.)



301 times in sixteen years, and cases in which the abdomen has been punctured more than a hundred times are not very rare. The results of hepatic cirrhosis, of cirrhosis complicated by chronic peritonitis, and of chronic peritonitis alone, may be arranged in this order from the point of view of the severity of the prognosis. Thus, in 31 cases of uncomplicated hepatic cirrhosis the average duration of life after the first appearance of ascites was 98.6 days; in 12 cases of cirrhosis complicated with chronic peritonitis, 288 days; and in 9 cases of uncomplicated chronic peritonitis, 624 days (Ramsbottom<sup>1</sup>). In milky ascites the prognosis is bad. In rare cases ascites spontaneously disappears, and great diminution has been noted during an attack of fever.

**Treatment** in the first instance should be directed to the underlying cause, if this be known and amenable to cure, for example, syphilis of the liver or heart disease. In simple chronic peritonitis and hepatic cirrhosis no known drug exerts any direct action on the morbid process. The palliative treatment consists in attempts to diminish the passage of fluid into the peritoneal cavity and to effect its removal. A restricted intake of fluids or a "dry diet" has been recommended, but is usually very disappointing. The results of a salt-free diet are not very striking.

The means for the removal of fluid from the abdominal cavity fall under three heads: (1) By paracentesis, (2) by diuretics, and (3) by purgatives.

1. *Paracentesis abdominis* is indicated when the abdominal distension causes pain or vomiting, when upward displacement of the diaphragm gives rise to dyspnoea, or to collapse and œdema of the lung, as shown by moist sounds at the bases behind, and when there is considerable diminution in the amount of urine. In cirrhosis, hematemesis or signs of incipient delirium tremens indicate the advisability of tapping an ascitic abdomen.

The abdomen is most advantageously tapped below the umbilicus in the middle line. If from adherent omentum no fluid is withdrawn in this position, the trocar and cannula must be introduced elsewhere. It has been recommended that the middle point of a line drawn from the anterior superior spine of the ilium to the umbilicus should be chosen, and that in order to avoid wounding the cecum or liver the left side should be selected. In rare instances fatal hemorrhage has followed puncture in this position from a wound of the deep epigastric artery (Boidin,<sup>2</sup> Lian<sup>3</sup>). This accident may be suspected if, on withdrawing the cannula, pure blood comes in spurts, and should be met by ligature of the vessel.

Before the abdomen is tapped the urinary bladder should be emptied, and the site of the puncture percussed and be found to be dull. The patient should lie on his back with the head slightly raised; the skin in the neighborhood of the intended puncture should be cleaned and rendered aseptic. If necessary, the skin may be anesthetized by ethyl

<sup>1</sup> *Medical Chronicle*, Manchester, 1906, xlv, 7.

<sup>2</sup> *Bull. Soc. anat.*, Paris, 1903, lxxviii, 415.

<sup>3</sup> *Ibid.*, 1907, lxxxii, 665.

chloride and cocaine injected under the skin at the site of puncture. A comparatively small cannula should be used, so as to remove the fluid slowly. Rapid removal of fluid may lead to faintness. The sterilized trocar and cannula should then be introduced, the trocar withdrawn, and the shield fixed in position by plaster. The fluid is then allowed to run away through a thin india-rubber tube. This takes some hours to drain away, and during this period the abdomen may be protected by a cradle, and a many-tailed bandage or a binder should be kept comfortably tight over the abdomen. If the flow stops before the abdomen has been fairly well evacuated, the india-rubber tube should be "milked," starting from the cannula. When the fluid has finally ceased to run, the cannula should be withdrawn and the small wound closed by a pad of absorbent cotton-wool soaked in collodion. The abdomen should be bandaged or tightly strapped with adhesive plaster, to prevent rapid accumulation of the fluid and flatulent distension. In some instances good results have followed the injection through the cannula, after the abdomen has been nearly emptied, of a dram of adrenin chloride, 1 to 1000, in an ounce of water. It has been shown experimentally that injection of adrenin into the peritoneal cavity increases absorption of fluid (Fleischer and Loeb<sup>1</sup>). Apart from wounding a bloodvessel in the abdominal wall, there are very few dangers connected with paracentesis. In extremely rare instances acute pulmonary oedema has occurred. Wounding of the abdominal viscera should be avoided if proper care be taken. Repeated tapping may set up some degree of chronic peritonitis; acute peritonitis is, with ordinary attention to aseptic precautions, very rare. Prolonged or permanent drainage is not advisable.

2. *Diuretics* are disappointing and their use should not be persisted in when there are indications that paracentesis is necessary. They sometimes succeed after paracentesis, probably because the kidneys are then in a better position to act; for a large ascitic effusion exerts pressure on the renal veins and thus chronic venous engorgement is induced. The diuretics employed are numerous, and the use of any one will to some extent be determined by the cause of the ascites. In heart cases Baillie's or Addison's pill, containing digitalis, squill, and mercury, is commonly used; citrate of caffeine, diuretin, or theocin combined with digitalis may also be given. In ascites due to other causes acetate, citrate, or tartrate of potash, spirit of juniper, copaiba resin (in capsules), and urea may be tried.

3. *Purgation*.—Moderate purgation by calomel or jalap and salts, such as tartrate of potassium or sulphate of magnesium and sodium combined, may be tried; but drastic purgatives, such as elaterium and gamboge, should be avoided, as the patient's strength may be seriously impaired. Such treatment in the past has been thought to have purged patients to death.

**Operative treatment** in tuberculous peritonitis and hepatic cirrhosis is considered elsewhere (pages 535, 729).

<sup>1</sup> *Jour. Exper. Med.*, 1910, xii, 288.

**Hemoperitoneum.**—The presence of pure blood free in the peritoneal cavity is somewhat rare, and must be distinguished from blood-stained ascitic effusions. The causes of intraperitoneal hemorrhage are: (1) Rupture of ectopic gestation; this is the most frequent cause; of 20 cases of intraperitoneal hemorrhage examined by Dudgeon and Sargent,<sup>1</sup> 17 were due to this cause. Rupture of a lutein hematoma may cause extensive intraperitoneal hemorrhage. (2) Traumatic rupture of the spleen, liver, or mesentery. (3) Rupture of aneurisms of the cœliac axis, or of the superior mesenteric, hepatic, or other intra-abdominal arteries. Aneurisms of the abdominal aorta usually rupture behind the peritoneum in the first instance, but may subsequently leak into the peritoneal cavity. (4) From leakage of a hemorrhagic or vascular new-growth, such as an angiosarcoma of the liver or adrenals. (5) From rupture of varicose or dilated veins; thus, most profuse hemorrhage may occur from rupture of a dilated vein on the surface of a subperitoneal fibromyoma; Wallace<sup>2</sup> has collected 16 cases. Rupture of a varicose vein in the broad ligament is rapidly fatal, but is fortunately extremely rare. The writer has seen a large quantity of blood in the peritoneal cavity from traumatic rupture of a vein in peritoneal adhesions. (6) From rupture of a hemorrhage into the suprarenals. (7) In very rare instances repeated peritoneal hemorrhages may occur without any known cause. In Cheeseman and Ely's<sup>3</sup> case the abdomen was tapped forty-three times in five years and then spontaneous cure occurred. Both pleuræ had previously presented recurrent hemorrhagic effusions.

Intraperitoneal hemorrhage, although sterile at first, rapidly becomes infected. Of Dudgeon and Sargent's 20 cases, only one was completely sterile, and that was operated upon two hours after the onset; the organism isolated by these observers was a white staphylococcus. This explains (a) the fever which may follow intraperitoneal hemorrhage, and was formerly referred to the absorption of fibrin-ferment; and (b) the onset, if the patient survived sufficiently long, of peritonitis.

**Symptoms.**—Sudden pain which marks the extravasation of blood into the peritoneal cavity is followed by faintness, rapid and feeble pulse, restlessness, sighing respiration, vomiting, attacks of colicky pain, bloodlessness and extreme pallor, sweating, and collapse. In some cases, for example, rupture of an aneurism, death occurs at once. In other cases, especially when the blood is poured out less rapidly, the symptoms may imitate those of peritonitis due to perforation of a gastric ulcer.

**Sequelæ.**—If the patient is not operated upon and survives, acute general peritonitis will follow, unless, indeed, the extravasation be sufficiently localized to become encysted and form a peritoneal sanguineous cyst (see page 738).

**Diagnosis.**—In the presence of symptoms of internal hemorrhage and a history of recent and severe trauma the diagnosis is easy. On the other hand, ruptured ectopic gestation may so closely resemble acute

<sup>1</sup> *Lancet*, 1905, i, 474.

<sup>2</sup> *Brit. Med. Jour.*, 1910, ii, 1226.

<sup>3</sup> *Amer. Jour. Med. Sci.*, 1899, cxviii, 166.



perforative peritonitis that the condition is not suspected until the abdomen is opened. When collapse occurs in a patient known to have an intra-abdominal tumor the occurrence of hemorrhage may be suspected.

**Prognosis** is best in ruptured ectopic gestations, but it is necessarily fatal in ruptured aneurisms and eventually, of course, in leaking malignant growths.

**Treatment.**—When the cause is a ruptured extra-uterine gestation or spleen the only course is removal of the ruptured organ.

**Choleperitoneum.**—Rupture of the bile passages with effusion of bile into the peritoneum usually sets up peritonitis, because the bile is commonly infected; but escape of aseptic bile into the peritoneal cavity need not cause inflammation; and in rare instances large bilious effusions result. This condition was named choleperitoneum by D  v  ,<sup>1</sup> and in 1906 Beaudet<sup>2</sup> collected 47 cases due to rupture of a hydatid cyst which either before or after the rupture was in communication with a bile duct. The abdomen usually enlarges slowly, but it may do so rapidly. There is no fever, and jaundice does not occur. The effusion is very apt to recur, and several tapplings may be required. Johansson<sup>3</sup> has collected 5 cases, and Wolff<sup>4</sup> has published 3 more examples of copious effusion of bile into the peritoneum, associated with cholecystitis but without any perforation of the biliary tract. Possibly the effusion is connected with the occasional presence of Luschka's canals or hernial protrusions of the mucosa into the wall of the gall-bladder (Johansson).

### ACUTE DIFFUSE PERITONITIS

Although acute peritonitis means acute inflammation of the peritoneum, the term is used to describe cases showing the clinical effects of acute infection of the peritoneum, namely, septicemia and toxemia, in which there may be very little or no manifest inflammatory reaction on the part of the peritoneum. These cases are more suitably described as "acute peritoneal infection." Thus, although it may sound paradoxical, the most severe cases of peritoneal infection often show the least evidence of inflammatory reaction. Acute diffuse peritonitis is not necessarily universal and coextensive with the whole area of the peritoneum. Strictly speaking, cases of acute peritonitis might be divided into (1) circumscribed, (2) diffuse or spreading, and (3) universal or total. But in practice acute peritonitis is usually considered as either (1) circumscribed or localized, or (2) general or diffuse. There is some unavoidable vagueness about the terms general and diffuse as descriptive of the extent of the peritonitis seen at an operation; thus the words employed may be meant to imply universal infection and inflammation of the peritoneum throughout the whole of the abdomen, or only that

<sup>1</sup> *Rev. de chir.*, Paris, 1902, xxvi, 67.

<sup>2</sup> *Gaz. des h  p.*, Paris, 1906, xlix, 1065.

<sup>3</sup> *Rev. de chir.*, Paris, 1912, xlii, 892.

<sup>4</sup> *Berlin. klin. Wchnschr.*, 1912, xlix, 2355.

at the time of the operation the peritonitis was not strictly localized. It has, therefore, been suggested that the term universal should be employed instead of general, and progressive instead of diffuse. The term diffuse will be employed here.

**Pathogeny.**—Although chemical poisons, such as turpentine, croton oil, and nitrate of silver, when introduced into the peritoneal cavity of animals can set up acute inflammation, it is safe to assume that in practice all cases of acute peritonitis in man are due to infection.

The mere entry of microorganisms into the peritoneal cavity is not alone enough to produce peritonitis. The defensive powers of the peritoneum, viz., the phagocytic action of the endothelial and other cells, the bactericidal power of the peritoneal fluid depending on the presence of antibodies, and absorption—which destroy and remove the invading bacteria—are able to prevent the production of inflammation. With regard to absorption from the peritoneal cavity, it should be explained that, while the removal of bacteria in comparatively small quantities and their destruction in the lymphatic glands and other organs prevent the onset of peritonitis and are therefore beneficial, the passage of large numbers of virulent bacteria into the general circulation, which occurs when the endothelial cells of the peritoneum are damaged, gives rise to a grave and often fatal bacteriemia. Death from “shock” after perforation may in all probability be explained in this way. The absorptive powers of the peritoneum also militate against peritonitis by removing fluid in which microorganisms might multiply. The defensive powers of the peritoneum have been divided by Andrewes<sup>1</sup> into those which are physiological, or the “first line of defense,” and those which come into play when inflammation is set up, or the “second line of defense.” These two lines of defense merge into each other, for example, in phagocytosis, but the formation of fibrinous adhesions which localize the infective focus is a frankly inflammatory process.

When the defensive powers of the peritoneum are inhibited or prevented from exerting their full effects, bacterial invasion is enabled to set up peritonitis. Factors which reduce the resistance of the peritoneum, such as the sudden entrance of poisonous fluids, drying or trauma during the course of an operation, and possibly cold, may interfere with the absorptive and bactericidal powers of the peritoneum. The presence of solid bodies, such as particles of food, feces, blood-clot, concretions, or foreign bodies, or of ascitic fluid, may protect the bacteria, provide a nidus for their multiplication, inhibit absorption, and so enable them to produce their toxins and set up inflammation of the peritoneum.

**Etiology.**—Acute diffuse peritonitis may be (1) primary or (2) secondary.

1. The term *primary idiopathic peritonitis* has been employed in two senses. Formerly it was used to imply that inflammation attacked the peritoneum alone, the rest of the body being healthy, and that its cause and origin were unknown. Peritonitis formerly thought to be

<sup>1</sup> *General Pathology and Bacteriology of Acute Peritonitis. System of Medicine* (Allbutt and Rolleston), 1907, iii, 897.

due to rheumatism or to cold comes under this heading. More recently, since it has been recognized that acute peritonitis is practically always infective, the term primary peritonitis has been applied by Flexner<sup>1</sup> to cases in which, as there is no local focus in the abdomen to account for the infection of the peritoneum, it is assumed that microorganisms have reached the peritoneum by the blood- or lymph-stream. Hematogenous peritonitis occurs as a terminal infection in chronic nephritis, arteriosclerosis, cancer, and other conditions which reduce the bactericidal power of the blood. Some cases of peritonitis complicating erysipelas or other infections, and about half of the instances of pneumococcic peritonitis, would also appear to be primary and so of hematogenous origin. Since a minute local focus, such as a microscopic abscess in the appendix, may be easily overlooked, a most exhaustive postmortem examination is necessary before a case of primary idiopathic peritonitis can be accepted, and many writers are somewhat unwilling to admit its existence. Of this, however, there can be no doubt, and probably about 10 per cent. of the fatal cases of general peritonitis are of this nature. It occurred in 12 out of 106 cases examined by Flexner and in 9 out of 105 cases at the Massachusetts General Hospital (Manahan<sup>2</sup>). The infection is usually single; thus out of Flexner's 12 cases no bacteria were found in 2, in 9 there was a single infection, and in 1 a mixed infection.

2. *Secondary peritonitis*, in which infection is due to some local lesion either in or in the immediate neighborhood of the abdomen, accounts for the great majority of cases of acute diffuse peritonitis.

(a) Wound or operation introducing infection into the peritoneal cavity, *e. g.*, after herniotomy. To this group Flexner applies the term exogenous. But it must, of course, be remembered that postoperative peritonitis may be due to bacterial infection derived from the viscera.

(b) Due to infection derived from the abdominal viscera. This may depend on gross perforation of their walls or be due to inflammation allowing microorganisms to pass through the intestinal walls. This is Flexner's endogenous group. It will be convenient to mention the affections of the abdominal viscera which may cause acute peritonitis.

*Stomach*.—Perforation of a gastric ulcer; perforation due to rapidly growing, soft, and necrosing carcinoma; acute suppurative (or phlegmonous) gastritis; acute gastritis due to corrosive poisons.

*Small Intestines*.—Traumatic rupture, perforation by sharp foreign bodies; perforating ulcers, duodenal; jejunal peptic ulcer, occurring in cases of gastrojejunostomy, especially, it is said, after the anterior operation; typhoid ulcer (peritonitis in rare instances occurs in the absence of any gross perforation); uremic ulcer; acute enteritis; strangulation, kinking, volvulus, intussusception; internal hernia; infarction.

*Appendix*.—Perforation as a result of acute infective inflammation; from rupture of an abscess in the walls of the appendix or in its neighborhood, or from acute appendicitis.

<sup>1</sup> *Philadelphia Med. Jour.*, 1902, ii, 1019.

<sup>2</sup> *Boston Med. and Surg. Jour.*, 1905, clii, 345.



*Colon*.—Perforation, traumatic or by a foreign body from within. Perforating ulcer, stercoral or dysenteric; in connection with carcinoma, either from rupture of a distension ulcer or leakage through necrosing growth. Extremely acute inflammation, in strangulation, volvulus, intussusception. Wounds, perforation of the rectum by a bougie, or by the nozzle of an enema syringe.

*Gall-bladder*.—Acute, phlegmonous, or gangrenous cholecystitis. Rupture of an inflamed gall-bladder.

*Liver*.—Rupture or leakage of an abscess or of a suppurating hydatid cyst. Abscess may be multiple and due to arterial infection, suppurative pyelphlebitis or cholangitis. In new-born infants phlebitis of the umbilical vein gives rise to peritonitis.

*Spleen*.—Rupture of an abscess, or of a suppurating infarct.

*Mesenteric Glands*.—Rupture of a suppurating lymphatic gland into the general cavity of the peritoneum.

Ulceration and perforation of the *urinary bladder* or of sacculi in connection with it.

*Suppurating and gangrenous ovarian cysts*.

*Pyosalpinx* and infection spreading from the Fallopian tubes. Riedel<sup>1</sup> has shown reasons for believing that salpingitis is a more important cause of general peritonitis under ten years of age than in adults.

*Perforation of the uterus by a sound*.

*Rupture of an abscess* into the peritoneal cavity, especially of a perpendicular abscess; this may follow rough manipulation. It is remarkable how rarely erysipelas or suppuration in the abdominal parietes gives rise to peritonitis; this probably depends on the lymphatics being independent. Although peritonitis may lead to infection of the pleuræ, an empyema hardly ever ruptures into the abdominal cavity. Inflammation readily spreads from the pancreas to the peritoneum of the lesser sac. Retroperitoneal suppuration, such as that due to tuberculous ostitis of the spine or to renal calculi seldom infects the peritoneum.

As giving the relative importance of the various starting-points of acute peritonitis, Benda's<sup>2</sup> 446 cases of acute diffuse peritonitis examined after death may be referred to. The vermiform appendix was the starting-point in 115 cases, the stomach and duodenum in 68, the rest of the intestine in 118, the female genitals in 81, the gall-bladder in 10, the kidney and urinary bladder in 10, the pancreas in 2, the spleen in 1; 35 were unknown, 4 were postoperative, and 2 hematogenous.

The *sex* and *age* incidence depend on those of the commonest causes of peritonitis, perforating gastric ulcer and pelvic infections being the most frequent etiological factors in women, and appendicitis in children and young males. In 200 fatal cases at St. George's Hospital there were 107 males and 93 females; the average age of the 200 cases was thirty-two years, being 34.26 in the males and 29.3 years in the females. In infants acute peritonitis is usually due to infection from the umbilicus.

<sup>1</sup> *Arch. f. klin. Chir.*, Berlin, 1906, lxxxi, 186.

<sup>2</sup> Quoted in *A System of Surgery*, von Bergmann, von Bruns, and von Mikulicz, translation, vol. iv, 165.

**Bacteriology.**—In the following account the results obtained by Dudgeon and Sargent will be freely utilized. A large number of microorganisms have been found in human peritonitis. In many instances there is a mixed infection, and difficulty arises in apportioning the share that the organisms present have taken in producing peritonitis. The organisms found in peritonitis are in nearly all instances morphologically the same as those commonly present in the healthy intestine.

*Bacillus coli* is very commonly found, and considerable discussion has taken place whether its importance is commensurate with its frequency. It has been regarded as the all-important factor in peritonitis, and, on the other hand, it has been thought that the *B. coli*, being more hardy than other bacteria, may overgrow them and so be found postmortem to the exclusion of other microorganisms which are the real factors in producing peritonitis. It is naturally found most often in cases of peritonitis due to infection from the alimentary canal, and is very frequently present in association with some other organism. In 56 cases of peritonitis due to bowel infection, Flexner found the *Bacillus coli* in 43, in pure culture in 8, and in association with other organisms in 35. Dudgeon and Sargent,<sup>1</sup> as the result of bacteriological examination of 270 cases, came to the conclusion that the colon bacillus is the most important factor, and that it is found in the largest number of fatal cases. Its virulence varies greatly, and while less dangerous than the streptococci and *Bacillus pyocyaneus*, it is more frequently present. With mixed cultures a very virulent peritonitis is set up.

A white *staphylococcus*, which is not the same as the *Staphylococcus pyogenes albus* described by Rosenbach, and has often been regarded as due to contamination from the skin, and is probably Welch's *Staphylococcus epidermidis albus*, has been found by Dudgeon and Sargent to be the first organism to appear in the peritoneal cavity in cases of early peritonitis, and to pass through the walls of the inflamed intestine before more virulent organisms. They found it in 108 out of 258 peritoneal lesions.<sup>2</sup> It gives rise to an exudation rich in phagocytes, and thus exerts a protective action against more virulent microorganisms.

*Streptococci* are found in a considerable percentage of the cases. Flexner found them second in order of frequency both in his primary and secondary groups of peritonitis. As streptococci are among the normal saprophytes of the intestinal canal, it is natural that they should be commonly present in cases of peritonitis due to intestinal lesions; but it must be remembered that the *Streptococcus pyogenes* has not been found normally in the alimentary canal, and that streptococci found in the peritoneum are not necessarily *Streptococcus pyogenes*, and may be the saprophytes of the intestine (Andrewes and Horder<sup>3</sup>). Peritonitis due to *Streptococcus pyogenes* is the most severe and fatal form; there is little or no local reaction, the phagocytes being powerless against the virulent microorganisms which, as shown by Buxton's<sup>4</sup> experiments,

<sup>1</sup> *The Bacteriology of Peritonitis*, Constable & Co., London, 1905.

<sup>2</sup> *Lancet*, 1906, ii, 1337.

<sup>3</sup> *Ibid.*, 1906, ii, 708.

<sup>4</sup> *Jour. Med. Research*, 1907, xvi, 39.

are rapidly absorbed into the circulation and give rise to fatal bacteriemia in the course of twenty-four to forty-eight hours from liberation of their endotoxins.

*Staphylococcus pyogenes aureus* was found by Flexner in 15 out of 34 cases of exogenous peritonitis, being in pure culture in 12 and mixed in 3. It was present in 3 only in 39 cases of endogenous peritonitis. It gives rise to a virulent form of peritonitis.

*Bacillus pyocyaneus* is responsible for a certain number of cases of acute peritonitis, and ranks next to the *Streptococcus pyogenes* in its virulence. It does not produce green pus in the peritoneal cavity, as it often does in a local abscess. Dudgeon and Sargent have shown that *Bacillus coli* will not grow in the presence of *B. pyocyaneus*.

*Bacillus typhosus* has been found in a few cases of peritonitis due to perforation of typhoid ulcers, and even after rupture of the spleen. But it is combined with saprophytic organisms, and it is doubtful what importance should be attached to its presence.

Other organisms such as *Bacillus lactis aërogenes* (Churchman<sup>1</sup>), *B. influenzae* (Hull and Fisch<sup>2</sup>), *B. proteus*, *B. anthracis*, are occasionally found. With regard to anaërobic organisms, there has been a good deal of discussion; Veillon and Zuber and Tavel and Lanz conclude that anaërobic organisms are of importance in the production of appendicitis and peritonitis, while Dudgeon and Sargent employed strictly anaërobic precautions in a number of cases of appendicitis and in other varieties of peritonitis, but failed to find anaërobic organisms except in one case of gangrenous appendicitis with abscess in which *Bacillus aërogenes capsulatus* was found in addition to *B. coli* and a streptococcus. As the result of the presence of anaërobic organisms the peritonitic exudate may become putrid.

It may be well to summarize the data at our disposal as to the bacteriology of peritonitis due to various anatomical lesions. In perforative peritonitis due to gastric ulcer the pneumococcus and a streptodiplococcus, an organism of low virulence (Dudgeon and Sargent), have been thought to be the responsible organisms. In perforation of the small intestine the *B. coli* and streptococci, and in appendicitis various organisms, especially streptococci (Low, Lartigau), *B. coli*, and diplococci have been regarded by different observers to be the causal organisms. In puerperal peritonitis and peritonitis in the new-born streptococci are most often the responsible organisms.

**Morbid Anatomy.**—The appearances necessarily vary with the causes and stages of acute peritonitis. In the most rapidly fatal cases, there may be little or no morbid change. In other cases the earliest visible change is congestion of the small bloodvessels of the peritoneum; this is not uniformly distributed, but is naturally best marked and at first confined to the starting-point of the inflammation and to the omentum which is often adherent to the focus of infection. Further, it is more marked on the visceral than on the parietal peritoneum, and is in most instances not diffuse, but is confined to longitudinal lines which

<sup>1</sup> *Johns Hopkins Hosp. Bull.*, Baltimore, 1911, xxii, 116.

<sup>2</sup> *St. Louis Med. Rev.*, 1903, xlviii, 55.



correspond with the spaces left between contiguous and distended coils of intestine. The next change is the exudation; at first there is slight dulling of the smooth peritoneal surface, which appears finely granular, and on scraping yields a little fibrin. This fibrin is sticky and as it increases in amount glues the intestines together and collects in the triangular chinks left between adjacent coils. At first the fibrin is thin and clear, but it becomes opaque, and may be yellow or even of a green tint. Large masses of fibrin may eventually form and show a somewhat spongy or reticulated structure.

The fluid portion of the exudation, usually comparatively small, may in some instances be considerable (several quarts). It collects between the intestinal coils; during life it is often mainly in the loins, but after death it is more commonly seen in the pelvis. Its characters vary much in different cases: it may be (1) serous; (2) serofibrinous, turbid, with pieces of fibrin floating in it, and of a specific gravity of 1.018 or upward; (3) fibrinous; (4) fibrinopurulent; (5) purulent; (6) sanious; (7) putrid, due to the presence of putrefactive anaërobic organisms, such as the *Bacillus aërogenes capsulatus*. In such cases there may be free gas in the peritoneal cavity without any perforation of the hollow viscera. In virulent streptococcic infection there is a little thin, odorless fluid; in gonococcic infection there is a dry, fibrinous exudate with hardly any pus or serum; in pneumococcic peritonitis the exudate resembles that in a pneumococcic empyema, and in *B. coli* infections there is a thick, creamy pus. In some instances of peritonitis secondary to cholecystitis the exudation may be bilious without any gross perforation of the biliary tract (Wolff,<sup>1</sup> Johansson<sup>2</sup>).

The *progressive fibrinopurulent form of peritonitis* described by Mikulicz is transitional between circumscribed and diffuse peritonitis. There is a gradually extending area of foci of pus enclosed in fibrinous adhesions and in rare instances the whole of the peritoneal cavity may be involved. Rupture of an encysted collection of pus may cause purulent peritonitis.

The intestines are in a state of paralytic distension, the walls somewhat swollen, œdematous, and softened from inflammation so that the peritoneum readily strips off and the intestine may rupture if pulled upon. In children there may be retrograde intussusceptions produced during the death agony. The peritoneum may show scattered small hemorrhages, and small extravasations of blood are not uncommon in the ovaries. The omentum is often adherent to the starting-point of the peritoneal infection, *e. g.*, the appendix.

The lymphatics become filled with exudations and cells, and infection is, as shown by Durham<sup>3</sup> both experimentally and by observations on fatal cases of peritonitis in man, conveyed to the lymphatic glands in the anterior mediastinum; these glands are swollen, reddened, and contain microbes. As the result of toxic absorption the solid viscera, such as the liver, pancreas, spleen, kidney, show cloudy swelling of their cells and areas of focal necrosis. Rarely other serous membranes,

<sup>1</sup> *Berlin. klin. Wehnschr.*, 1912, xlix, 2355. <sup>4</sup>

<sup>2</sup> *Rev. de chir.*, Paris, 1912, xlv, 892.

<sup>3</sup> *Jour. of Path. and Bacteriol.*, Edinburgh and London, 1897, iv, 361.

especially the pleuræ, are inflamed as the result of a concomitant infection—an acute polyorrhomenitis. In prolonged cases, especially in pneumococcic and puerperal peritonitis, local abscesses may form. These if left alone may perforate in various directions, into hollow viscera, or even externally at the umbilicus.

*Microscopically* the endothelium of the peritoneum, especially of the omentum, early shows proliferative changes; the cells enlarge; their nuclei become swollen and divide by direct and then by indirect nuclear division. The cells ("macrophages" of Metchnikoff) thus produced vary in size, but some are indistinguishable from lymphocytes. The surface of the endothelial cells is covered by a layer of fibrin containing leukocytes, and there is small round-celled infiltration of the subendothelial tissues. Coarsely granular eosinophilic cells constitute a considerable proportion of the immense number of leukocytes attracted to the bloodvessels of the part; this local accumulation is correlated with the diminution of eosinophilic cells in the peripheral circulation (Opie<sup>1</sup>). At a later stage the cell infiltration of the underlying structures becomes more intense and extensive, and the peritoneal endothelium is destroyed. If the inflammatory process be short-lived the endothelium survives and the fibrin is eventually absorbed, so that the formation of adhesions is prevented. If the inflammatory process be continued the endothelial cells are destroyed and adhesions form.

The exudation and fibrin present on the surface of the peritoneum are protective by (a) enabling phagocytosis and bacteriolysis to take place, (b) by blocking up the lymph channels and so preventing absorption from the peritoneal cavity, and (c) by preventing the passage of microorganisms from the lumen through the walls of the inflamed intestine.

**Cytology.**—As the result of experimental bacterial infection, Durham found a leukopenic stage lasting an hour, the normal hyaline and eosinophilic cells disappearing from the peritoneal fluid, which becomes increased in amount, while the lymphocytes remain. The disappearance of the cells is due to their being collected into balls on the surface of the peritoneum, especially on the omentum. In very virulent infections the leukopenic stage may persist until death. According to Dudgeon and Ross's<sup>2</sup> experiments the first cells found in the exudation are either small lymphocytes or coarsely granular eosinophiles; subsequently there are polymorphonuclear leukocytes (Metchnikoff's "microphages," microxyocytes) which are derived from the blood; these cells have been found by Beattie<sup>3</sup> to diminish in number in non-fatal cases in from forty-eight to sixty hours after the onset, but to persist until death in fatal cases. They are active phagocytes, as are also the mononuclear cells (macrophages) derived from the endothelial cells of the peritoneum, which, however, according to Buxton,<sup>4</sup> are unable to digest bacteria effectively in the absence of an early and marked polymorphonuclear reaction. Dudgeon and Ross state that the coarsely granular eosinophilic

<sup>1</sup> *Transactions of the Association of American Physicians*, 1904, xix, 136.

<sup>2</sup> *British Medical Journal*, 1905, ii, 1043.

<sup>3</sup> *Journal of Pathology and Bacteriology*, Edinburgh and London, 1903, viii, 129.

<sup>4</sup> *British Medical Journal*, 1907, ii, 1422.

leukocytes (megakaryocytes), which are usually regarded as non-phagocytic, are, in the early stages of peritoneal infection, among the important if not the most important phagocytes.

The peritoneal exudation is not infrequently free from microorganisms and from phagocytes containing bacteria, while the surface of the intestine and the omentum shows their presence. This observation is important in the consideration of the question of "chemical" peritonitis, for it is clear that the peritoneal exudate may be sterile, and so suggest a non-bacterial peritonitis. The wall of the intestine shows small-celled infiltration around the vessels and fibrinous and serous exudation; the nerve cells of Meissner's, Auerbach's and the solar plexuses show degeneration (Laignel-Lavastine<sup>1</sup>).

**After-results.**—Acute peritonitis leaves behind it some slight thickening and opacity of the peritoneum; in cases in which blood has been extravasated pigmentation may be due to altered blood-pigment. As the result of organization of fibrin, adhesions are commonly seen, but it is remarkable how completely they may disappear in course of time.

**Symptoms.**—The signs and symptoms of diffuse peritonitis vary quite widely in different cases; this depends on the cause of the peritonitis and on the virulence of the infecting organisms. It will, therefore, be best to give a very brief description of a common form of peritonitis, then to detail the manifestations that may occur in the various forms of peritonitis, and lastly to refer to special forms, pneumococcic, gonococcic, and puerperal.

The course of diffuse acute peritonitis can be most satisfactorily sketched by a short account of an ordinary case of perforative peritonitis. There is a sudden onset with agonizing burning pain and a feeling that something has given away; this is rapidly followed by collapse. These symptoms are due to the perforation. The abdomen is rigidly contracted and extremely tender. Tympanitic distension from escape of large quantities of gas into the peritoneal cavity is very rare at this stage. There is widespread and very severe pain which is exaggerated by any movement, so that respiration is costal and shallow, and there is frequent vomiting. The collapse passes off in a few hours, and for a time the patient appears fallaciously better; this period of latency or "stage of repose" (Symonds<sup>2</sup>) may be prolonged by the administration of opium or morphine. But when the disease is allowed to run its natural course, symptoms reappear and those of peritoneal inflammation become unmistakable; the abdomen gradually becomes distended, the legs being drawn up to relax the abdominal parietes, the arms usually lying above the head. There is extremely severe and constant pain, which becomes exaggerated in paroxysms and is made worse by the slightest movement, such as micturition; vomiting is frequent; the tongue becomes dry, the mouth parched, there is constant thirst, the temperature is somewhat raised, the pulse of high tension, wiry and rapid, the face pinched, anxious, and generally pale, and its aspect that of grave toxemia and of progressive exhaustion. As time goes on the

<sup>1</sup> *Arch. de méd. expér. et d'anat. path.*, Paris, 1905, xvii, 54.

<sup>2</sup> *British Medical Journal*, 1899, i, 520



abdominal distension increases, the pulse becomes thready, more rapid, and weaker, the skin is cold and clammy, and the extremities icy and blue, although the internal temperature may be considerably raised. Restlessness and anxiety persist, there is little or no sleep, the mind is usually clear to the end, but occasionally there is wandering or delirium. Pain, tenderness, and vomiting occasionally pass off shortly before death, which may be sudden from cardiac failure, but sometimes there is profuse vomiting just before death, and aspiration of the foul fluid into the lungs may be the last straw.

**The Clinical Picture.**—The underlying factors which are responsible for the clinical manifestations are: (1) Acute inflammation involving an extensive area. (2) Paralysis of the muscular walls of the intestines. (3) Septicemia and toxemia, due to the absorption of microorganisms and toxins from the peritoneal surfaces and of toxins from the paralyzed intestines. (4) Abstraction of water from the tissues.

The *onset* varies with the cause. When this is perforation of a hollow viscus, as in gastric or duodenal ulcer, the moment of the accident can usually be absolutely fixed. In typhoid fever, however, perforation may not be marked by sudden and acute pain, and from dulling of the patient's powers of perception the existence of acute peritonitis may be an anxious problem. In the late stage of renal disease, intra-abdominal new growths, cirrhosis, pulmonary tuberculosis, etc., the onset and even the existence of peritonitis may be latent and not suspected during life. In some cases, especially after abdominal operations and in intestinal obstruction, the onset of peritonitis is so gradual that it cannot be definitely fixed. In puerperal and occasionally in slowly progressive forms of peritonitis, such as may occur in connection with appendicitis, the development is gradual and insidious. With an acute onset there is more or less shock due to the damage done to the peritoneum by the sudden entry of the contents of an abscess or of a hollow viscus into the abdominal cavity. This shock may prove fatal before peritonitis has had time to develop.

The *facial aspect* of advanced peritonitis is characteristic, and has been described as "a composite photograph of hemorrhage, pain, and infection" (Crile). The face is pinched, the skin being tightly drawn over the bones, the eyes sunken and surrounded by dark rings, the skin gray or somewhat livid from failure of the circulation, and the expression anxious. This is the abdominal or Hippocratic face. In early stages, however, there may be nothing characteristic in the face, and the cheeks may be flushed.

The tongue, at first furred and moist, subsequently, from the loss of fluid and absence of saliva, becomes shrivelled, dry, and stained by the vomit. Unless the mouth is carefully and constantly cleaned, sordes collect on the teeth. There is complete loss of appetite, and extreme thirst.

*Position.*—The patient lies on his back, the shoulders raised, and the thighs flexed so as to relax the abdominal walls as far as possible. The arms and head are tossed about and manifest the mental restlessness, but the rest of the body is kept as still as possible.

*Pain* is practically a constant symptom. It is only in cases in which a terminal peritonitis supervenes in the course of a chronic exhausting disease, such as gastric carcinoma or renal disease, or of an acute disease, such as typhoid fever, in which the mental faculties are greatly dulled, that pain is absent. The pain may be continuous with that of the causal perforation; in other forms of peritonitis it comes on more gradually, and steadily increases until it becomes intolerable. It is constant, but becomes worse from time to time, the exacerbations probably depending on movements of the intestines; vomiting, cough, or any kind of movement aggravates the pain, and accordingly the patient keeps the abdomen and trunk absolutely still, and holds the arms above the head, while the movements of the diaphragm are greatly restricted.

The pain is general all over the abdomen, but may be more marked in some one part, such as the umbilicus or the right iliac fossa, and may thus correspond with the starting-point of the disease. But this may be fallacious; for example, the pain may be most marked in the appendix region in perforated duodenal ulcer, and in pelvic appendicitis the pain is not uncommonly referred to the umbilicus. Toward the end the pain may disappear; this may be in part the result of the effusion and of intestinal paralysis, which prevent the intestines from rubbing against the parietal peritoneum; in part to the continued effect of toxemia on the exhausted sensorium. The diminution or disappearance of pain, therefore, does not mean that there is any improvement.

*Tenderness.*—Opinions differ as to cutaneous hyperesthesia. In order to test accurately for it, the skin, without any of the underlying tissues, should be carefully picked up between the finger and thumb. Head<sup>1</sup> states emphatically that it is absent, and Sherren<sup>2</sup> has never found it in general peritonitis due to appendicitis. Hale White,<sup>3</sup> however, says that it is often present, and H. Robinson<sup>4</sup> who found it in some cases suggests that it is only when the parietal peritoneum becomes inflamed that it appears. In acute peritonitis the abdominal reflexes are not exaggerated, as they would be if the tenderness were cutaneous (Head). Tenderness of the deeper tissues is due to implication of the parietal peritoneum and its somatic nerve supply in the inflammatory process. The tenderness gets progressively worse, and may be so extreme that the patient cannot bear the weight of the bedclothes; it is universal and corresponds with the extent of the peritoneum, being elicited by rectal and vaginal examination. Rectal examination may show ballooning of the rectum.

*Rigidity of the Abdominal Walls.*—In the early stages the muscles are firmly contracted from spasm, and there may even be retraction; this is most marked in perforative peritonitis. In strong and muscular men the rigidity is prominent and lasts for a considerable time; in fact, in very acute cases it may persist until the end. In women with very flaccid abdominal parietes there may be no appreciable rigidity. Although this muscular defense is one of the most common events in the course of

<sup>1</sup> *Brain*, 1893, xvi, 94.

<sup>3</sup> *Manual of Medicine* (Allchin), 1903, v, 490.

<sup>4</sup> *Quart. Jour. Med.*, Oxford, 1907-08, i, 406.

<sup>2</sup> *Lancet*, 1903, ii, 816.

acute peritonitis, it may be absent throughout; this is seen in gonococcic peritonitis, and even in cases in which there is no special atrophy of the abdominal muscles. This absence of rigidity is more likely to occur in non-perforative cases and in the somewhat slowly progressive fibrino-purulent peritonitis. As a result of this muscular spasm, the abdomen becomes more or less immovable; this is a valuable sign of peritonitis, but movement of the abdomen does not prove that peritonitis is absent. Muscular rigidity passes off when the patient is anesthetized.

*Tympanites.*—Except in the fulminating and rapidly fatal cases, the early rigidity gradually passes off, and in about forty-eight hours is succeeded by abdominal distension; in less acute cases this may be delayed for a day or two longer. The abdominal distension may come on more rapidly after rupture of the stomach and escape of gas into the abdominal cavity. The tympanites or meteorism of peritonitis is due to distension of the paralyzed intestines with flatus; to a slight degree accumulation of liquid feces in the dilated intestines, and inflammatory peritoneal exudate contribute to it. Its onset is naturally favored by a flaccid condition of the abdominal parietes, such as may result from parturition, abdominal tumors, or ascites. The abdomen becomes prominent, hyperresonant, and the skin tight, stretched, and shiny. Abdominal movement is abolished.

The distension pushes up the liver in such a manner that the normal relation of that organ to the parietes is altered, and very little of it remains in contact with the body wall; in extreme instances the thin edge of the liver looks upward and backward instead of downward and forward. As a natural consequence, the hepatic dulness is diminished or obliterated, and this without any free gas in the abdominal cavity. Absence of liver dulness must not be taken as evidence of perforative peritonitis. The diaphragm is pressed up, so that the lower lobes of the lungs become œdematous and partially collapsed, and the breathing thus further embarrassed. The apex of the heart may be displaced upward.

The intestinal paralysis, which is one of the most important factors in acute peritonitis, is probably nervous and due to reflex shock; it may be increased by œdema and inflammation of the muscular walls and the local action of toxins on the neuromuscular apparatus of the intestinal wall. But from the rapid onset of distension in some cases of peritonitis, before inflammation can have spread sufficiently into the intestinal wall to produce muscular paralysis, this is certainly not the only factor concerned. Distension is lessened by copious vomiting. The distension may force a coil of intestine into a hernial sac, and so suggest that the symptoms are due to strangulation of the bowel, but examination will show that the hernia is reducible.

Percussion is painful; when there is distension the note is usually tympanitic, but certain areas, especially the flanks, may be dull due to collections of peritoneal exudate or to the intestine being full of fluid. In rare instances a friction-rub can be heard. On the other hand, a valuable sign of intestinal paralysis is the entire absence of any gurgling sound when the abdomen is auscultated for five minutes at a time (Greig Smith).



Edema of the abdominal wall is extremely rare; when it does occur it is usually in connection with a localized collection of pus, for example, appendicular abscess. It is not a sign of diffuse peritonitis.

*Vomiting* is one of the most characteristic and, next to pain, the most constant manifestations. It may be absent, however, especially in young children. In the early stages, of which it is often the first symptom, it is probably a reflex result of irritation of the peritoneum, although it has been regarded as due to the action of toxins on the medulla. In the later stages it is, like the vomiting of acute obstruction, due to a reflux flow of fluid into the stomach from the paralyzed intestines. That it depends on paralysis of the intestines and overflow into the stomach of their stagnating contents is supported by the rule that it is less prominent or absent in cases in which the bowels act or in which there is diarrhea, as in puerperal peritonitis; further, washing out the stomach prevents the vomiting. It is commonly excited by taking fluid to relieve the urgent thirst.

The vomited materials are first those of the stomach, then those of the upper part of the small intestine containing easily recognizable bile, and lastly feculent or stercoraceous matter of an extremely offensive character. In severe cases the vomit is often brown or dark in color from the presence of blood. The fluid is brought up with comparatively little effort, welling up into the mouth. The amount varies somewhat, but is much less than in mechanical obstruction. It is rather remarkable that vomiting occurs in cases of perforation of the stomach. The movement entailed in vomiting exaggerates the abdominal pain. Nausea is common, there is a bad taste in the mouth, and foul gas may be belched up. In the later stages retching may be substituted for vomiting. The loss of fluid entails continual thirst.

*Hiccough*, when it occurs, usually comes on in the late stages of peritonitis when the abdomen is considerably distended. It is a reflex phenomenon, due to implication of the phrenic nerve.

*Rigors* are not common; they are seen in some cases of puerperal peritonitis, and in the prolonged form of progressive fibrinopurulent peritonitis.

*Constipation* is the rule, and, from intestinal paralysis, is often so marked, both for flatus as well as for feces, as to give the case the aspect of acute mechanical obstruction. An enema will, however, usually bring away some fecal matter in acute peritonitis without any improvement in the patient's condition; this does not hold good for mechanical obstruction. So constant is constipation in acute peritonitis that cases in which it is absent or in which the bowels can be made to act may generally be regarded as hopeful. In puerperal peritonitis, however, diarrhea, due presumably to some peculiar form of toxin, is the rule. In other forms, except in that due to pneumococcic infection, it is exceptional.

*Respiration*.—As diaphragmatic and abdominal movements are greatly reduced or abolished, the respiratory excursions mainly depend on the intercostal muscles. The upper parts of the lungs are therefore employed to a larger extent as a means of compensation for the impaired

movements of the lower lobes, and some of the extraordinary muscles of inspiration come into action. The respirations are painful, shallow, and considerably increased in rate (40 to 50 per minute); coughing and deep breaths are restrained.

The *pulse* varies in character at different stages of the disease. It is nearly always regular, quickened, and becomes progressively more rapid, being 100 to 120 in the early stages, and becoming running, 170 or uncountable, toward the end. In some instances the pulse may be little if at all accelerated, although there is extensive purulent peritonitis; this has been ascribed to interference with toxic absorption from blocking of the stomata and lymphatics, but is not necessarily a sign that the patient is improving. There is no correspondence between the rate of the pulse and the temperature; the temperature may be low and the pulse extremely rapid. The pulse is small, hard, and wiry in the early stages; Crile,<sup>1</sup> who found the average blood-pressure in 20 cases to be 166 mm. Hg., ascribes the small volume to the accumulation of blood in the splanchnic area and the hardness to reflex stimulation of the vasomotor centres from the peritoneum. In collapse and in the later stages the blood-pressure falls and the pulse becomes thready.

The *temperature* is so extremely variable as to be of little or no value in diagnosis or as to the degree and gravity of the peritonitis. There is usually a more considerable difference between the rectal and the surface temperatures, such as the axillary, than in other diseases; this is connected with the stagnation of blood in the splanchnic area and the correspondingly small amount of blood in the cutaneous vessels.

In perforative peritonitis the initial shock nearly always depresses the temperature; this is most noticeable in typhoid fever, in which the writer has seen a fall of eight degrees. But this is not an absolute rule; the variation probably depends on how much of the peritoneum is inundated by the contents of the bowel. The form of infection may influence the temperature, and a particularly virulent microbic invasion may so paralyze the power of resistance that there is less febrile reaction than in a less severe infection. In the vast majority of the cases of diffuse peritonitis the temperature is raised in some period of its course; it may be raised continuously, usually not to any great extent, and very seldom above 104°. A relatively high temperature, especially in the early stages, is more likely to occur in the healthy and vigorous. A persistently low temperature may depend on the severity of the infection and on failure of the organism to react, and is a grave sign.

*Blood.*—There is anemia, but the erythrocyte count is not greatly diminished; probably the concentration of the blood accounts for this. In 16 cases examined by Da Costa, the average was 3,970,000 reds, and the color index 0.78. In fulminating cases in which the resisting powers of the body are paralyzed by the intensity of the toxemia, leukocytosis is absent and there may be leukopenia. In less severe peritonitis there is a leukocytosis which may be extremely marked. It is of the ordinary polymorphonuclear neutrophile form. According to Locke<sup>2</sup>

<sup>1</sup> *Blood Pressure in Surgery*, Philadelphia, 1903.

<sup>2</sup> *Boston Med. and Surg. Jour.*, 1902, cxlvii, 287.

and Gulland<sup>1</sup> the glycogenic reaction seen in the polymorphonuclear neutrophiles is much more trustworthy, for it is present in cases of peritonitis with such a "brutal" infection that leukocytosis does not appear. Cabot<sup>2</sup> lays stress on the importance of the increase of the fibrin network (hyperinosis) in the diagnosis from mechanical obstruction for this increase does not occur in obstruction, while leukocytosis does.

*Blood-cultures.*—Although the fatal results of peritonitis are usually considered to depend upon septicemia as well as on toxemia, and although organisms can often be found after death in the heart's blood, it does not appear that the presence of organisms in the blood during life has been proved. In this connection it may be pointed out that in human septicemia pyogenetic cocci are demonstrated with difficulty in the blood, thus contrasting with experimental peritoneal infection and septicemia in animals. Libman<sup>3</sup> found that in 25 cases of peritonitis, mainly of intestinal origin, the blood was sterile, although in some instances the blood-cultures were made shortly before death.

The *urine* is scanty, high-colored, and may contain a small quantity of albumin, diacetic acid, and acetone. The most important point, however, is the large quantity of indican, which may rise from the normal 5 to 20 mg. in adults to 150 mg. Indicanuria takes some twelve to twenty-four hours to appear after the onset of perforative peritonitis.

According to Lenmander, the urine contains the organisms responsible for the peritonitis. Their presence, especially as he states they may appear within twenty-four hours of the onset of the disease, may possibly in the future be of some value in directing the treatment. From the presence of peritonitis over the bladder micturition is painful, and usually urine is retained. Occasionally, on the other hand, micturition is more frequent than normal.

The *mental faculties* are often clear to the end, but sometimes they are somewhat obscured by the progressive toxemia. Sleeplessness is necessarily the rule, headache is common, and great anxiety and a painful form of restlessness are often present.

*Death* may be quite sudden from cardiac failure, due to the action of toxins on the heart muscle, and may follow almost immediately after copious vomiting. Death sometimes comes gradually from progressive asthenia.

The *duration* is very variable and depends on the cause and on the nature of the infection, the previous state of the patient, young and vigorous, or old and the subject of some exhausting disease, and on the treatment. Thus, in the most virulent and fulminating forms, as in some cases of appendicular and puerperal infection, death may occur in thirty-six to forty-eight hours from the onset, whereas the more usual and less severe forms generally last four, five, or even more days. A previously healthy boy may live through several days with severe peritonitis, while a patient with carcinoma of the stomach may only survive the onset of perforative peritonitis for eighteen to twenty-four

<sup>1</sup> *Brit. Med. Jour.*, 1904, i, 880.

<sup>2</sup> *Examination of the Blood*, 1904, p. 282.

<sup>3</sup> *Johns Hopkins Hospital Bulletin*, 1906, xvii, 221.



hours. In pneumococcic peritonitis the duration may be considerably prolonged, as the peritonitis may become localized into residual abscesses, so that the symptoms abate without disappearing. Progressive fibrino-purulent peritonitis may go on for weeks.

**Pneumococcic peritonitis** presents some rather special features. The disease is much commoner in children than in adults. It may occur very early in life; Gossage<sup>1</sup> reported 4 fatal cases of primary pneumococcic peritonitis in infants under three months, and Dudgeon and Sargent its occurrence in a male infant aged seven weeks. Under the age of fifteen years it occurs more often in girls than in boys; among 234 cases in children 62, or 27 per cent., were males, and 172, or 73 per cent., females (Barling<sup>2</sup>), but after that age its incidence is equal in the two sexes. The following channels have been regarded as enabling the pneumococci to reach the peritoneum: (1) Through the blood-stream, the organisms being absorbed from pneumococcic foci in the thorax or possibly from the throat or ear; (2) from the stomach and intestines in inflammatory conditions, appendicitis, or foci in the abdominal viscera; (3) from the pleuræ through the diaphragm; and (4) through the Fallopian tubes. Probably infection of the peritoneum occurs by different channels in different cases; but when associated, and in children, Rischbieth<sup>3</sup> finds that this is almost always the case, with other pneumococcic lesions, such as pneumonia, pleurisy, pericarditis, polyorrhomenitis, meningitis, otitis, and arthritis, it is probably septicemic. Diffuse peritonitis is rare in pneumonia; in 4454 cases<sup>4</sup> of lobar pneumonia in patients over ten years of age in the hospitals of London there were 11 fatal cases, or 0.25 per cent. In most cases the peritoneum has been previously healthy; in a few instances there has been ascites due to cirrhosis or to chronic nephritis (Sevestre and Aubertin<sup>5</sup>). Pneumococcic peritonitis was primary, that is, the chief or only focus of infection in 47 out of 74 cases, and in 34 of these 47 cases the peritonitis was encysted (Lenormant and Lecène<sup>6</sup>).

In about half the cases the peritonitis is encysted or localized; in the other half it is diffuse or widespread. A localized abscess may either be primary or a result of diffuse pneumococcic peritonitis. The exudate is like that of a pneumococcic empyema; it is highly fibrinous and prone to coagulate, yellowish green in color, and odorless. The character of the exudation renders thorough drainage of the peritoneum difficult. In some instances, however, a much more fluid exudate has been found. When the peritonitis is localized an abscess results which is usually below the umbilicus, and is particularly prone to point at the umbilicus.

*Clinically* the disease may run a very acute course and prove fatal in two or three days, or death may not occur until the sixth or seventh day. There may be the following stages: (1) Without prodromal symptoms

<sup>1</sup> *Proceedings of the Royal Society of Medicine*, London, 1908, i (Med. Sect.), 64.

<sup>2</sup> *Practitioner*, London, 1912, lxxxviii, 557.

<sup>3</sup> *Quart. Jour. Med.*, Oxford, 1910-11, iv, 205.

<sup>4</sup> Statistics of Hadley, Pasteur, Fawcett, Owen, Gossage, *Proceedings of the Royal Society of Medicine*, London, 1908, i, (Med. Sect.), 61 et seq.

<sup>5</sup> *Bull. et mém. Soc. méd. d. hôp.*, Paris, 1906, xxiii, 215

<sup>6</sup> *Rev. de gyn. et de chir. abdom.*, Paris, 1905, ix, 225.

there is an acute onset with vomiting, followed by signs of peritonitis, often mainly in or near the pelvis, so that appendicitis may be diagnosed. (2) After a few days the symptoms subside, the temperature falls, but diarrhoea is usually present, and for this reason typhoid fever may be suspected. (3) A prolonged stage in which residual abscesses may form, usually in the upper part of the abdomen, giving rise to continued fever and imitating tuberculous peritonitis. Herpes labialis may occur.

The *prognosis* in encysted pneumococcic peritonitis is fairly good, but it is very grave in the diffuse form; thus Rohr<sup>1</sup> found that recovery occurred in 86 per cent. of the encysted and in only 11 per cent. of the diffuse form.

**Gonococcic Peritonitis.**—The gonococcus alone, *i. e.*, in pure culture, is capable of setting up diffuse peritonitis (Cushing<sup>2</sup> and Hunner<sup>3</sup>). When the normal resistance of the peritoneum is diminished by menstruation or by cold, gonococci in the Fallopian tubes have a better chance of infecting the peritoneum. Gonococci enter the peritoneum from the ostia of the Fallopian tubes, but gonococcic peritonitis has followed leakage from a pyosalpinx during removal by operation. In males infection is said to travel up the lymphatics of the spermatic cord.

The disease is very rare in men and its frequency in women has not yet been established by extensive statistics; but diffuse gonococcic peritonitis is not common. In 1907 Goodman<sup>4</sup> collected 75 cases, but only 30 of these had been established by bacteriological examination at autopsy or operation. It may attack girls under puberty, and it is highly probable that it is often overlooked. It usually follows or precedes menstruation, and may appear shortly after delivery. The lesions are comparatively slight; there is a dry, fibrinous exudate without pus or serum, and the peritoneum is uniformly injected in the diffuse cases.

*Clinically*, gonococcic peritonitis comes on suddenly with great severity, which usually becomes greatly mitigated in twenty-four or forty-eight hours. Comby<sup>5</sup> speaks of the condition as one of peritonism rather than of peritonitis. It appears to be more fatal in children than in adults; the mortality in children has been estimated at 20 per cent. It may imitate appendicitis, as it mainly affects the lower part of the abdomen. Abdominal distension is usually not marked, and muscular rigidity is absent. Its existence should be suspected in the presence of gonorrhœa when the peritonitis is mainly in the lower part of the abdomen. At the onset of the disease the gonorrhœal discharge may be slight, and as its existence is often firmly denied careful examination is necessary to avoid overlooking it. It is usually agreed that the patients should not be operated upon, but in 20 cases in which laparotomy was performed there were only four deaths (Goodman).

**Puerperal Peritonitis.**—The infection gains entry through tears or wounds of the genital passages, and is more frequent in primiparæ than

<sup>1</sup> *Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1911, xxiii, 658.

<sup>2</sup> *Johns Hopkins Hospital Bulletin*, 1899, x, 75. (This article contains the detailed history of gonococcic peritonitis.)

<sup>3</sup> *Ibid.*, 1902, xiii, 247.

<sup>4</sup> *Annals of Surgery*, 1907, xlvi, 111.

<sup>5</sup> *Arch. mal. d. enfants*, 1901, iv, 512.

in multiparæ. It is not uncommon in criminal abortion. The infection spreads from the genital organs by the lymphatics, and may be localized or widespread in the peritoneal sac. The organism is most commonly *Streptococcus pyogenes*, but staphylococci or the gonococcus may be the causal agent. The exudation may be purulent, sanious, or putrid.

*Clinically* there is grave intoxication and usually diarrhœa; vomiting is less prominent than in other forms; meteorism is marked, partly no doubt from the weakened abdominal walls; and a high mortality, which may be correlated with the presence of *Streptococcus pyogenes*. At its onset the lochia may be offensive and the mammary secretions be suppressed. Complications are prone to occur, and include septicemia, empyema, pericarditis, arthritis, and phlebothrombosis.

**Diagnosis.**—In characteristic cases the association of the prominent symptoms of acute pain, tenderness, distension, and immobility of the abdomen, vomiting, constipation, prostration and collapse, together with the history, make the existence of acute peritonitis clear. But in many cases the decision is far from easy. When peritonitis supervenes late in the course of chronic nephritis it may be almost latent, when it occurs in typhoid fever it may be difficult to distinguish from tympanites, and in acute intestinal obstruction its manifestations are combined with and obscured by those of the primary disease. Further, the symptoms may be almost entirely masked by opium or morphine. In some cases the majority of the signs and symptoms may be absent, although there is advanced peritonitis. This masked or latent form of peritonitis may occur in patients in the last stages of exhausting diseases, such as cancer. After operations on the abdomen the only evidence of peritonitis may be vomiting and a rapid pulse.

**Diagnosis of Acute Peritonitis from Conditions Simulating It.**—In hysteria a condition of peritonism may occur and give rise to considerable anxiety, as the diagnosis between it and genuine peritonitis occurring in a hysterical patient may be difficult. The history of the patient and any concomitant nervous symptoms must be taken into account. As an important point the occurrence of exactly similar attacks in the past should be specially noted. In such cases there is cutaneous hyperæsthesia; deep tenderness is not more marked than the superficial hyperæsthesia, and may disappear if the patient's attention be distracted.

Severe *colic*, whether due to lead, constipation, or the passage of a gall-stone or renal calculus, may to some extent imitate acute peritonitis. In colic there is, as a rule, no real tenderness, and the pain may be relieved by firm pressure. In severe lead colic there may, however, be tenderness, but the pupils are often unequal and there may be tenderness over the vagus in the neck (T. Oliver<sup>1</sup>). In a doubtful case with abdominal tenderness the possibility of lead-poisoning should always be considered. In colic due to the passage of a calculus vomiting occurs, but it is rare in the other forms. The history and examination for evidence of lead-poisoning, renal, or hepatic disease should be carefully considered. A raised temperature at the onset is strongly in favor of

<sup>1</sup> *System of Medicine* (Allbutt and Rolleston), 1906, ii, part i, 1045.



peritonitis and against ordinary colic. Colic, however, is more likely to be confused with the causes of peritonitis—such as appendicitis—than with the disease itself. The rare and puzzling condition of enteralgia may also imitate peritonitis; here again the history of repeated similar attacks is of importance. Extremely acute enterocolitis is accompanied by the same collapse as in peritonitis, but there is marked diarrhœa and the pain is of a colicky character.

*Tympanites* should be readily distinguished from acute peritonitis by the absence of tenderness and vomiting.

In acute mechanical intestinal *obstruction* acute peritonitis supervenes after some three or four days, and, conversely, acute peritonitis produces intestinal paralysis and the symptoms of obstruction, so that the diagnosis as to the primary lesion may be difficult. In acute obstruction the temperature is not raised, and the abdomen is not tender or rigid before the onset of secondary peritonitis. In mechanical obstruction feces and wind are not passed, while in peritonitis an enema will often bring some away. In mechanical obstruction vomiting is more profuse; the pain is colicky and not continuous, as in peritonitis.

Extensive *hemorrhage* into the peritoneum, usually due to rupture of an ectopic gestation, may imitate perforative peritonitis very closely; in fact, the manifestations in both instances are those of shock. A similar clinical condition of peritonism may follow hemorrhage into the mesentery, torsion of an undescended testis, of an ovarian cyst, of a floating kidney, or of a wandering spleen. Rupture of an abdominal aneurism and embolism of the superior mesenteric artery have imitated acute peritonitis (Osler).

*Acute hemorrhagic pancreatitis* may imitate acute perforative peritonitis; great collapse, abdominal distension, complete constipation, and vomiting follow the sudden onset of pain in the epigastric region. If the abdomen be opened, turbid fluid and fat necrosis may be found. It may be noted, however, that fat necrosis may be due to the escape of pancreatic fluid through the perforation of a duodenal ulcer,<sup>1</sup> so that its discovery, although almost pathognomonic of pancreatitis, does not absolutely exclude perforation. In pancreatitis there is extreme feebleness of the pulse, the temperature is often not raised, and the symptoms are more suggestive of mechanical obstruction than of peritonitis.

Acute inflammatory conditions in the thorax, such as *lobar pneumonia* or *pleurisy*, may, especially at the onset before physical signs have appeared, imitate peritonitis. The sharp pain of pleurisy, the onset of which may wake a patient up in the night, has been mistaken for perforation of a gastric ulcer or of a gangrenous appendix. Difficulty is especially likely to arise in children in whom the appearance of the physical signs of pneumonia, particularly when apical, is often much delayed. In pneumonia the respirations may be jerky and grunting. The rigidity of the abdominal muscles sometimes seen in pneumonia, especially in children, relaxes between the respirations, and may even disappear on prolonged and deep pressure (Clogg<sup>2</sup>), while the referred

<sup>1</sup> White, *Archives of the Pathological Institute of the London Hospital*, 1906, i, 48.

<sup>2</sup> *Clinical Journal*, London, 1906, xxix, 93.

pain of thoracic disease is mainly superficial and not increased on deep pressure, as in peritonitis. The temperature may be of some assistance; low at the onset of perforative peritonitis, it then rises, but may fall after some hours, although the patient's condition is not improved. It thus differs from the continuous fever of pneumonia. Indicanuria is in favor of peritonitis. Tuberculous peritonitis in rare cases comes on with such acute symptoms in children as to imitate very closely peritonitis due to appendicitis.

In women about the menstrual period sudden acute pain may imitate perforation of a hollow viscus or rupture of an ectopic gestation. The symptoms pass off, as a rule, but are alarming enough at the time. The underlying cause has been thought to be hemorrhage into the ovary. In one case attended by great temporary collapse the real cause appeared to be synthetic drugs taken to relieve the pain on the first day of the period.

*Uremia* may imitate diffuse peritonitis, and it must be remembered that uremic ulceration of the intestine may lead to perforative peritonitis, and that hematogenous peritonitis may supervene in chronic renal disease.

In very rare instances acute abdominal symptoms imitating appendicitis or even peritonitis supervene in *Addison's disease* (Nattan-Larrier<sup>1</sup>) and appear to be allied to the vomiting in that disease.

*Pernicious malaria*, due to estivo-autumnal parasites, may cause symptoms suggesting peritonitis. The diagnosis depends on the detection of the parasite.

When the presence of peritonitis has been determined it is most important to diagnose the cause and to decide whether it is due to perforation of a gastric, duodenal, or an intestinal ulcer, to appendicitis, to rupture of an abscess, and, if so, where, to gonococcic or pneumococcic infection, and so on; for on the correct diagnosis of the cause depends the site of the abdominal incision in the first instance. As bearing on the cause of peritonitis in any given cause the following points may be taken into consideration:

*Age*.—In children peritonitis of sudden onset is most commonly due to fulminating appendicitis; but pneumococcic and gonococcic peritonitis must be considered.

*Sex*.—In young women perforated gastric ulcer and pelvic infection are the most common causes.

*History*.—Symptoms of dyspepsia in young women at once suggest a perforated gastric ulcer, while in patients about fifty years of age carcinoma of the stomach with perforation should not be forgotten. When peritonitis comes on suddenly in a patient who has had gastro-enterostomy done for gastric ulcer, the possibility of perforation of a peptic jejunal ulcer should be thought of. The existence of typhoid fever, advanced kidney disease, or of a pelvic abscess will indicate the probable starting-point of the peritoneal infection.

The position in which the pain is first felt should be considered, but

<sup>1</sup> *Clinique médicale de l'Hôtel-Dieu*, Paris, 1906, v, 250.

it is by no means a certain guide, for, although pain starting in the right iliac fossa naturally suggests appendicitis, pain in this situation may be due to perforation of a gastric or duodenal ulcer.

The sudden onset of peritonitis in a person in good health up to that time may be due, especially in children, to fulminating appendicitis, in young women to perforation of a latent gastric ulcer, and in men to perforation of a duodenal ulcer which is relatively more often latent than a gastric ulcer is in women.

**Prognosis.**—This is very bad. Statistics differ very much in the percentages of mortality, because, as has been pointed out, a case which at operation one surgeon may describe as diffuse another would regard as general or universal. In 100 cases at the London Hospital there were 70 deaths and 30 recoveries (Treves), but the different forms of peritonitis vary so much in their severity that no conclusion of any value can be obtained from statistics in which cases of the various kinds are indiscriminately included. Other things being equal, peritonitis is more fatal at the two extremes of life. The previous health of the patient, the presence of disease elsewhere, cachexia, and alcoholism, of course, have a bearing on the prognosis.

As the fatality of peritonitis depends on toxemia and septicemia, the prognosis to some extent varies with the degree of the toxic symptoms; the cases of acute peritoneal sepsis in which there is very little reaction on the part of the peritoneum are almost always fatal. Bad as the prognosis is in purulent peritonitis, it occasionally happens that the inflammation becomes localized and an abscess results. A very rapid pulse, a persistently low temperature, abdominal distension, and absence of leukocytosis are a bad prognosis.

From a bacteriological point of view peritonitis due to Dudgeon and Sargent's white staphylococcus is the most benign form, while that due to gonococci is comparatively mild. In pneumococcus peritonitis the prognosis is graver than in the forms just referred to, but is not so serious as in those now to be mentioned. The commonest cause of peritonitis is infection with virulent colon bacilli; if present alone in the peritoneal cavity at a distance from the infecting focus the outlook is bad; and if all the phagocytes are degenerated the prognosis is practically hopeless. If *B. coli* and the white staphylococcus are associated, the outlook is not so bad, but is still very serious. The *Streptococcus pyogenes* gives rise to the most acute and fatal peritonitis, and it is doubtful if any surgical procedure offers a prospect of success. Peritonitis due to the *B. pyocyaneus* is hardly less fatal (Dudgeon and Sargent).

The prognosis is almost necessarily fatal in perforative peritonitis unless operated upon; when operation has been performed the outlook is much better in traumatic rupture or bullet wounds of the intestine than in perforation due to disease. Similarly the prognosis is better in perforation of a gastric or duodenal ulcer than in perforation of an intestinal ulcer lower down, because, as shown by Cushing and Livingston,<sup>1</sup> the number of colon bacilli steadily diminishes from the ileocecal

<sup>1</sup> *Contributions to the Science of Medicine by the pupils of W. H. Welch, 1900.*



valve to the stomach, and the duodenum is often sterile when empty. The interval between the onset of peritonitis and the time at which the operation is performed has an important bearing on the prognosis; operation within twelve hours of the onset should be successful, while an interval of twenty-four hours makes the outlook very grave.

**Treatment.—Prophylaxis.**—Under this heading the briefest reference only need be made to the desirability of preventing or curing the causes of general peritonitis, such as gastric or intestinal ulceration, appendicitis, pelvic inflammation, and intra-abdominal abscesses. Among these the importance of timely surgical interference in acute appendicitis cannot be exaggerated. It is almost unnecessary to insist that strict precautions should always be taken to avoid the introduction of organisms into the peritoneal cavity when the abdomen is tapped for the relief of ascites or when laparotomy is performed.

Various prophylactic measures have been adopted in order to immunize the peritoneum against probable infection during the course of laparotomy. These measures are mainly based on Issaëff's<sup>1</sup> observation that injection of saline and other fluids into the peritoneal cavity produces a local leukocytosis, and so protects the animal against some forms of microbic infection; this ("Issaëff's resistance period") lasts four or five days. Buxton and Tracy<sup>2</sup> consider the protection mainly mechanical and due to blocking of the lymphatics by the inflammatory products, by means of which bacteriemia is prevented. Horse serum and nucleinate of sodium have been injected eleven or twelve hours before operation so as to induce a protective leukocytosis. The introduction into the abdominal cavity, at the end of operations on cases of peritonitis, of hot horse serum or salt solution has been advocated in order to increase leukocytosis; about 30 cc. of sterilized horse serum is poured through the drainage tube, and has given good results (Petit<sup>3</sup>).

**Surgical Treatment.**—The great majority of cases depend on infection from some local focus in the abdominal cavity, and are therefore rightly treated by removal of the cause. In the small minority of cases in which the infection is hematogenous, operative interference is not so necessary, but is required to drain a local abscess, as may be seen in pneumococcic peritonitis.

The objects of laparotomy are: (1) to remove the focus of infection, such as a perforated appendix, or to prevent continued reinfection, as is done in suture of a perforated ulcer; and (2) to give exit to the inflammatory exudate and if necessary provide efficient drainage. In order to prevent absorption of bacteria by the lymphatics of the diaphragm, the pelvis is lowered and the patient placed in the semi-sitting (Fowler's) position, at an angle of 35 to 40 degrees, both before operation and for some days afterward.

When the intestines are greatly dilated from paralysis, the danger of fatal toxemia from absorption of the foul contents of the bowel may be met by emptying the intestines. This can be done at the time of

<sup>1</sup> *Ztschr. f. Hyg.*, Tübingen, 1894, xvi, 287.

<sup>2</sup> *Jour. Med. Research*, Boston, 1907, xvii, 1.

<sup>3</sup> *New York Medical Record*, 1907, lxxi, 1017.

the operation by incising the bowel and expressing its contents, or, in more urgent cases, by inserting a Paul tube into the intestine and leaving it for some hours *in situ*. Other methods have been employed, such as injecting purgatives of magnesium sulphate by a syringe directly into the intestine during the operation (McCosh<sup>1</sup>), after removing some of its contents (Mayland<sup>2</sup>); by hypodermic injections of physostigmine or extracts of the posterior or infundibular lobe of the pituitary; by the administration of enemas, methods often quite unsuccessful; or by the administration of calomel in one-grain doses every hour until the bowels act; the calomel probably does good by its antiseptic action, as well as by leading to evacuation of the intestinal contents. Lawson Tait, who first advocated this line of treatment, gave saline purgatives. The purgative treatment of peritonitis has, however, met with considerable opposition both in the past and at the present time; it is useless when the intestines are paralyzed, and should only be adopted after operation and removal of the infecting focus. If employed before operation, it does harm by spreading the infection.

**Transfusion.**—In order to meet the urgent need for fluid and to combat collapse and toxemia, enemas of saline solution should be given; the introduction of saline solution either intravenously or subcutaneously has also been extensively employed. Of the last two the subcutaneous method is the more convenient and can be frequently repeated if needed. The solution should be of the strength of a dram of salt to a pint of water (0.6 per cent.) and should be introduced by gravitation, the fluid in the reservoir being kept at 115° F. In this way as much as 15 pints can be infused in the twenty-four hours (Barnard). By filling the vascular system, absorption of poisons from the peritoneal cavity is inhibited, the current of the stream between the peritoneal cavity and the circulation being reversed, the toxins already in the blood being diluted and their excretion by the kidney favored. Continuous administration of fluid per rectum has been employed with good results.

**Medical Treatment.**—The patient must, it need hardly be said, be kept in bed; the shoulders should be raised with pillows, so that the exudation will gravitate toward the pelvis rather than toward the diaphragm. If tenderness is extreme the bedclothes may be kept off the abdomen by means of a cradle. The abdomen should be manipulated as little as possible, both because of the tenderness and because infection may thus be spread. The mouth should be frequently cleaned and kept moist.

The administration of purgatives must be prohibited, for by promoting peristalsis they would increase the pain and spread the infection more widely in the peritoneal cavity.

No food or fluid should be given by the mouth, and the urgent thirst should be relieved by enemas of saline solution. In the later stages the administration of sterilized olive oil hypodermically has been advised. Vomiting may be treated by washing out the stomach. It is doubtful if bismuth, hydrocyanic acid, and drugs that calm an

<sup>1</sup> *Annals of Surgery*, xxvi, 691.

<sup>2</sup> *Brit. Med. Jour.*, 1899, i, 842.

irritable stomach in other diseases are worth giving. Tympanites is difficult to relieve; enemas containing turpentine may be tried; or a long rectal tube may be passed every three hours and left *in situ* for half an hour.

The administration of opium in acute peritonitis has given rise to a good deal of discussion, but it may safely be said that when given now it is for humanitarian reasons, and not with the expectation of any permanent benefit. The reasons for giving opium or morphine are the severity of the pain, and also, it was formerly urged, to keep the intestines at rest and so prevent further spread of the infective process throughout the abdomen. It is also given when the condition of the patient appears hopeless, so as to relieve pain and suffering. The objections to opium are weighty. It masks the symptoms in a marvelous manner, and so should never be given before a diagnosis has been made. But after a diagnosis has been arrived at, and especially when it is thought that the patient is too ill to stand operation, opium is not uncommonly given. Even in these conditions it is undesirable, for since it induces intestinal paralysis and inhibits phagocytosis (Dudgeon and Sargent<sup>1</sup>), it may just turn the scale against recovery.

Various local applications to the abdomen have been employed to relieve pain, such as hot and cold fomentations, the ice-bag, turpentine stupes, but often the slight pressure they exert gives rise to pain, and it is doubtful how much good is done in this way.

Collapse may be treated by the external application of warmth, bandaging the limbs, and the hypodermic injection of strychnine or pituitary extract; adrenalin has proved disappointing.

**Serum Treatment.**—In 25 cases of peritonitis due to appendicitis, treated by injections of the serum of a horse immunized against thirty-one strains of *B. coli*, recovery occurred in 9, or 36 per cent., and improvement was produced in all the others (Makins and Sargent<sup>2</sup>). Wilkie<sup>3</sup> treated 6 cases of very severe peritonitis with intravenous injections of human immune serum from patients recovering from similar infections and obtained 3 recoveries. Polyvalent antistreptococcic serum has been tried in numerous cases, especially in puerperal septicemia, unfortunately in the majority of cases without success.

### ACUTE CIRCUMSCRIBED PERITONITIS

Acute circumscribed or localized peritonitis may be conveniently divided into (1) non-suppurative and (2) suppurative.

*Non-suppurative acute circumscribed peritonitis* is extremely frequent and is due to extension of inflammation to the peritoneum. This is usually from organs in the abdominal cavity covered by peritoneum, such as the vermiform appendix, the intestines, the female genital organs, the gall-bladder and liver; but acute inflammation of the pleura

<sup>1</sup> *The Bacteriology of Peritonitis*, 1905, p. 188.

<sup>2</sup> *Transactions of the Clinical Society of London*, 1907, xl, 146.

<sup>3</sup> *Jour. Path. and Bact.*, Cambridge, 1910, xiv, 270.



or pericardium may spread through the diaphragm to the surfaces of the spleen and liver; the results of this process are comparatively often seen in adhesions found after death on both sides of the diaphragm. A good example is that produced by an infarct in the spleen. There is pain on breathing like that of pleurisy, local tenderness, and from organization of the localized exudate adhesions frequently follow.

*The chief clinical manifestation* is pain, which may vary in intensity but is confined to one area, and is made worse on pressure. A friction rub may be audible over the spleen or liver. In rather infrequent cases acute circumscribed peritonitis may, by producing local paralysis of a coil of intestine, set up acute obstruction; Mayo Robson<sup>1</sup> and Halsted<sup>2</sup> have described this as the result of acute cholecystitis. The main importance, however, of sharply circumscribed acute peritonitis lies not so much in its immediate effects as in results which it produces by the formation of local adhesions. By enclosing the affected area and shutting it off from the general peritoneal cavity, rupture of a perforating ulcer or of an abscess into the general peritoneal cavity may be prevented. On the other hand, the evil effects of a past attack of acute circumscribed peritonitis are shown by the occurrence of internal hernia due to strangulation of the intestine by bands and by "adhesion dyspepsia."

*The treatment* is mainly symptomatic and directed to the relief of pain by external applications, such as hot fomentations or ice, the patient's feelings being consulted as to which is most effective. Opium or belladonna may be applied to the abdomen, or, if the pain be obstinate, leeches may be employed. The underlying conditions should, when possible, be treated.

**Acute Pericolitis.**—This occurs in a number of conditions, and necessarily forms part of diffuse peritonitis and of various intraperitoneal abscesses and localized inflammations. As a descriptive heading, however, acute pericolitis should be confined to inflammation of the serous coat due to causes arising in the colon itself. Windscheid<sup>3</sup> first described cases under the name of pericolitis in 1889.

**Etiology.**—It may be due to causes which allow microorganisms to traverse the walls of the colon, such as acute inflammation, ulceration, injury, or the passage of sharp foreign bodies through the walls of the colon. There is often a history of previous constipation, but constipation is so common and pericolitis so comparatively infrequent that some further factor appears to be necessary. This additional factor is probably stercoral ulceration, especially in acquired diverticula of the colon. The writer has recorded several examples,<sup>4</sup> and Rixford<sup>5</sup> described a closely allied condition in which inflammation of the appendices epiploicæ is due to infection conveyed from the colon. It has been suggested that pericolitis is rheumatic, but so far without convincing evidence. As stercoral ulcers and false diverticula are more often present in the

<sup>1</sup> *Medico-Chirurgical Transactions*, London, 1895, lxxviii, 117.

<sup>2</sup> *Johns Hopkins Hospital Bulletin*, 1900, xi, 1.

<sup>3</sup> *Deutsch. Arch. f. klin. Med.*, Leipsic, 1889, xlv, 233.

<sup>4</sup> *Lancet*, London, 1905, i, 854.

<sup>5</sup> *California State Journal of Medicine*, October, 1904, p. 296.

sigmoid flexure and descending colon, pericolitis is commoner in these parts of the large intestine. It is spoken of as *perisigmoiditis* and *pericolitis sinistra*, but it may occur in the transverse or descending colon, especially at the flexures, where, from organization of adhesions (chronic pericolitis), the bowel may become narrowed, fixed, or kinked. Acute pericolitis may resolve, become chronic, or go on to the formation of a pericolic abscess.

The *symptoms* are pain, loss of appetite, occasionally vomiting, some elevation of temperature, and quickened pulse. There is constipation, which, indeed, is often concerned in the causation, and also an absence of the manifestations of colitis, such as loose stools and mucus. The skin over the area may be hyperesthetic, there is local muscular rigidity and deep tenderness, and in some instances an elongated tumor can be felt. Leukocytosis and indicanuria have been noted in some cases. The clinical manifestations, therefore, run into those of coprostasis or fecal accumulation with an acute exacerbation. The symptoms, apart from their position, are very much like those of appendicitis. Cases on the left side, or pericolitis sinistra, can be readily recognized, but on the right side the diagnosis from appendicitis is necessarily extremely difficult, and can hardly be regarded as established before operation has shown that the appendix is healthy. The *treatment* consists in rest in bed, soothing applications to the abdomen, and the relief of constipation, first by repeated enemas and subsequently by laxatives. The diet should be light and composed of food leaving little residue.

**Epiploitis.**—Epiploitis, or inflammation of the great omentum, is of course common in intraperitoneal inflammations on account of the tendency of the omentum to become attached to any focus of infection. It has been especially described as a result of abdominal operations in which silk ligatures have been applied to the omentum. Schnitzler<sup>1</sup> collected 28 cases after herniotomy, and it has also been met with two years after appendicectomy (Walther<sup>2</sup>). In some cases the condition has appeared long after the operation, there being a latent period of years. Cobb<sup>3</sup> has described epiploitis due to a needle which appeared to have entered from the umbilicus. The condition of the omentum varies; it may be thickened and rolled into a firm mass showing inflammatory changes, and it may be adherent to other structures, or free. In a woman under my observation two radical cures for hernia had been done in 1899 and 1900; in 1903 the appendix was removed, and about two months later a definite, firm abdominal tumor appeared on the left side and a hectic temperature developed, but on laparotomy there was no abscess formation; part of the omentum was rolled up into a round mass which microscopically showed developing connective tissue and some diminution in the number of fat cells. The inflammatory process may go on to the formation of an abscess.

The *symptoms* usually come on gradually, with fever, pain, constipation, and the presence of definite resistance or a tumor in the abdomen.

<sup>1</sup> *Wien. klin. Rundsch.*, 1900, xiv, 4.

<sup>2</sup> *Bull. et mêm. Soc. de chir. de Paris*, 1905, xxxi, 275.

<sup>3</sup> *Boston Med. and Surg. Jour.*, 1907, clvii, 18.

The tumor may be lumpy, firm, adherent to the abdominal wall, tender, and imitate a new growth. It may be chronic and eventually undergo resolution, but from contraction of adhesions the intestines may become kinked or otherwise obstructed. Epiploitis of this nature is rare, but if the conditions after which it occurs be borne in mind, the diagnosis should not be difficult.

**Treatment** in the early stage, when there is inflammation but not necessarily an abscess in the omentum, consists of soothing local applications. If fever persists and it appears probable that suppuration has occurred, laparotomy is the only course.

There are transitional forms between non-suppurative and suppurative acute circumscribed peritonitis. It is not very rare in appendicitis to see a tumor-like swelling, which gradually disappears in a few days without any evidence that pus has been discharged into the bowel. The swelling is probably due to adherent intestines, with some inflammatory exudate enclosed between the coils of the bowel. In other cases, *e. g.*, epiploitis, which at first show exactly the same features, an abscess eventually forms.

#### SUPPURATION IN THE MESENTERY AND OMENTUM

Suppuration in the mesentery is usually secondary to disease of the intestine. As the result of infection conveyed from the small intestine, a mesenteric gland may suppurate, or pyogenic infection may be engrafted on an old tuberculous adenitis. In cases of suppurative inflammation of the mesenteric veins there may be pus between the layers of the mesentery. Suppuration may also spread from the appendix into the mesentery. Barling<sup>1</sup> has published a series of cases, and has summarized the clinical aspect of the tumor; it is usually close to the umbilicus, mainly to the left side; when of considerable size it is practically fixed, but when of small size the swelling may not be palpable or if it can be detected is movable. Rupture of the abscess may set up general peritonitis.

**Omental abscesses** are rare. As has been mentioned above, suppuration may supervene after epiploitis. Thus, several abscesses have been found in the omentum more than a year after an operation.

#### PERIGASTRIC ABSCESS

By a perigastric abscess is meant one that is due to infection from the stomach but does not come in contact with the under surface of the diaphragm, and, strictly speaking, is therefore not included in the more striking category of subphrenic abscess. It is true that suppuration due to disease of the pancreas, gall-bladder, or liver may be in contact

<sup>1</sup> *Clinical Journal*, London, 1907, xxx, 62



with the stomach, but these abscesses should not be described as perigastric.

**Etiology.**—In exceptional instances a simple perigastric abscess may be due to a minute perforation in the stomach wall, such as is produced by a sharp foreign body, or to slight leakage from a gastric ulcer, but, generally speaking, perforation of a gastric ulcer is followed by a gaseous subphrenic abscess. A perigastric abscess occurs in from 3 to 5 per cent. of all cases of gastric carcinoma (Fenwick<sup>1</sup>) and is a late event. It is more often met with, so far as personal experience goes, in connection with rapidly growing and necrotic growths near the cardiac end; suppuration may then invade the left lobe of the liver. An abscess may form between the greater curvature of the stomach and the colon and then open into the large bowel, or may arise between the abdominal wall and the anterior surface of the stomach, and even point anteriorly or track down to the umbilicus. When a growth on the posterior wall of the stomach perforates, an abscess may form in the lesser sac of the peritoneum. The pus may be offensive, and if the abscess be opened during life, food may be discharged.

**Signs and Symptoms.**—A superficial perigastric abscess may be palpable as a definite swelling, and even give rise to a projection and to reddening of the skin. But usually, especially in gastric carcinoma, a perigastric abscess gives few physical signs; any increased resistance may be indistinguishable from that of the growth, and as fever occurs in 50 per cent. of the cases of gastric carcinoma (Osler and McCrae<sup>2</sup>) it is no proof of perigastric abscess.

**Diagnosis.**—It is practically impossible to diagnose between a perigastric abscess and the circumscribed form of phlegmonous gastritis, which is the same as an abscess in the walls of the stomach. A rapidly growing retroperitoneal sarcoma or hypernephroma may form a tender swelling in the left hypochondrium and imitate a perigastric abscess.

### PERICOLIC ABSCESES

Abscesses due to infection from the bowel may occur in the immediate neighborhood of the large intestine from a number of causes: (1) From ulceration of the mucous membrane of the bowel, due to dysentery, accumulation of feces (stercoral), or, more rarely, to other factors, and by perforation by foreign bodies, circumscribed peritonitis may be set up, and sometimes a localized abscess may result. The abscess may be intraperitoneal, and may open into the bowel (exogenous ulceration) or into the peritoneal cavity, or may be retroperitoneal. (2) The mucous membrane of false diverticula of the colon, which are more often found in connection with the sigmoid flexure, may, as the result of the accumulation of fecal material inside them, undergo ulceration; perforation of these diverticula may lead to an abscess in the immediate neighborhood. (3) Suppuration may occur in connection with a carcinoma of the large intestine. This may depend on perforation of the growth itself, on the

<sup>1</sup> *Cancer and Tumors of the Stomach*, 1902, p. 46.

<sup>2</sup> *Cancer of the Stomach*, 1900, p. 46.

passage of microorganisms through the floor of stercoral ulcers above the malignant stricture, or on perforation of these ulcers. The resulting tumor may be of considerable size, and on the right side must be differentiated from appendicitis with much inflammatory swelling, actinomycosis, and hyperplastic tuberculosis of the cecum. An abscess formed in connection with a malignant stricture of the bowel may extend and open into the urinary bladder or even externally; rupture into the peritoneal cavity, however, appears to be infrequent. (4) Small but sharp foreign bodies present in food may penetrate the wall of the colon and set up a fecal abscess in an appendix epiploica (Bland-Sutton<sup>1</sup>). This accident is more likely to occur in fat persons, for in thin individuals the foreign body more readily escapes into the peritoneal cavity.

The *symptoms* are abdominal pain, tenderness, resistance, local prominence or distension, and perhaps a tumor, usually on the left side and suggesting left-sided appendicitis or even a new growth. Constipation is commonly present, and also, not infrequently, vomiting. The abscess may increase in size and may rupture into the peritoneal cavity; the acute onset of peritonitis following on a period of pain and constipation may then suggest perforation above a malignant growth of the colon. Power<sup>2</sup> says that in some instances the abscess may become stationary, and from thickening of its walls give rise, for a time at least, to few clinical manifestations. The abscess may rupture into the intestine (Mayor<sup>3</sup>), or even into the urinary bladder, or externally (Patel<sup>4</sup>).

The *diagnosis* of these pericolic abscesses may be difficult, as from their comparative rarity some commoner condition, such as appendicitis in an unusual position, fecal accumulation, or malignant disease of the colon, may be suspected.

The *treatment* is purely surgical.

### RESIDUAL PERITONEAL ABSCESES

Residual peritoneal abscesses may occur in patients who have recovered from more or less general acute peritonitis. These abscesses may be found in any part of the abdomen, but are most often seen in the loins, pelvis, over the right lobe of the liver, or around the spleen. In tuberculous and pneumococcic peritonitis, and in suppuration in connection with the gall-bladder, abscesses may point at the umbilicus.

### RETROPERITONEAL ABSCESES

Suppuration behind the peritoneum may be due to many causes, and when starting in one spot may spread to a considerable distance along the fascial planes by the lymphatics. A retroperitoneal abscess may be in contact with the diaphragm. A psoas or iliac abscess due to tuberculous disease of the spine is, of course, retroperitoneal, but belongs

<sup>1</sup> *Lancet*, London, 1903, ii, 1148.

<sup>2</sup> *Brit. Med. Jour.*, 1906, ii, 1171.

<sup>3</sup> *Rev. méd. de la Suisse Rom.*, Genève, 1893, xiii, 421.

<sup>4</sup> *Rev. de chir.*, Paris, 1907, xxxvi, 420, 698.

to a somewhat different category, as does an iliac abscess due to calculous or tuberculous disease of the kidneys. Retroperitoneal suppuration may also be set up by disease of the bones of the pelvis or of the ribs. An abscess sometimes follows injury, especially in the neighborhood of the kidneys, and may be caused by minute rupture of viscera, or follow a hematoma. In other instances infection conveyed from the intestines to the retroperitoneal glands may result in the formation of an abscess. Perforation of viscera in situations where they are uncovered by peritoneum may be followed by retroperitoneal suppuration. Thus traumatic rupture, a penetrating bullet wound, or perforation of a stercoral ulcer in the colon may lead to a pericolic abscess, and an abscess around a carcinomatous stricture of the large bowel has been known to track into the thigh. Viscera entirely surrounded by peritoneum may, after contracting adhesions, perforate into the retroperitoneal tissues and set up an abscess; this is most commonly seen in connection with the vermiform appendix, but it also occurs in disease of the female genital organs. Retroperitoneal suppuration may be set up by infection introduced at operations, *e.g.*, herniotomy. These abscesses may rupture into the bowel or into other hollow viscera, such as the bladder or vagina.

**Clinical Picture.**—The constitutional manifestations—fever, rigors, loss of flesh, rapid pulse, and leukocytosis—are more constant than the local. There is often abdominal pain or uneasiness, while some deep tenderness on pressure may be present, and in some cases a palpable tumor. Focal signs may, however, be absent, and the condition may be thought to be typhoid fever, generalized tuberculosis, or some obscure septicemia. In some instances a diagnosis of an abnormally situated appendicular abscess may appear the most probable.

**Treatment** is purely surgical.

### SUBPHRENIC ABSCESS

Any abscess in contact with the under surface of the diaphragm, except when in the liver or in the spleen—the latter being rare—is spoken of as a subphrenic abscess. From a clinical standpoint there are two forms of subphrenic abscess: (1) without any contained air—simple subphrenic abscess; and (2) containing gas—the subphrenic pyopneumothorax. Their aspects are so different that separate descriptions are necessary, but their anatomy is the same, the differences between them depending on the nature of the contents, and the same cause may, in different cases, give rise to either of these forms of abscess. Thus an appendicular subphrenic abscess, although generally simple, may contain gas, and an abscess due to gastric ulcer, although usually gaseous, is not so in all instances. Nothnagel states that about half the subphrenic abscesses contain gas. In 59 cases of subphrenic abscess at St. George's Hospital, tabulated by Wahlby, 32 were gaseous and 27 non-gaseous.

**Subphrenic Abscess without any Gaseous Contents.**—**Etiology.**—The simple subdiaphragmatic abscesses which do not contain gas may in the first instance be due to pyogenetic infection derived from a solid



abdominal viscus in the neighborhood of the diaphragm; but suppuration may track up from the vermiform appendix or from the pelvis, *e.g.*, from a pyosalpinx. A simple subphrenic abscess may in rare instances arise in connection with ulceration, simple or malignant, of the stomach or colon, but, as a rule, the resulting abscess in cases of perforating gastric ulcer contains air.

The causes of simple subphrenic abscesses may be conveniently tabulated in the order of their frequency:

1. Appendicitis is the most frequent cause and the resulting abscess is nearly always on the right side, but a left-sided abscess may follow. The formation of a subphrenic abscess is a grave complication or sequel of appendicitis; thus among 86 fatal cases of acute appendicitis, subphrenic abscess occurred in 7, or 8.13 per cent. (Christian and Lehr<sup>1</sup>). In some cases of subphrenic abscess the causal appendicitis may remain latent and be quite unsuspected. Appendicitis may give rise to a subphrenic abscess in several different ways. (a) An appendix which is retrocecal, or runs up behind and to the outer side of the ascending colon and over the right kidney, may almost touch the right lobe of the liver; an appendicular abscess in this position (*i.e.*, the right kidney-pouch) has a very short distance to travel to reach the under surface of the diaphragm. (b) An abscess around the appendix may spread upward in the paracolic groove to the right kidney-pouch and extend upward over the liver and under the diaphragm; this is the intraperitoneal route. The abscess may be retrocolic or retroperitoneal, and track upward. An appendicular abscess situated in the pelvis may extend upward along the paracolic grooves on both the right and the left sides of the abdomen, and so give rise to bilateral subphrenic abscesses. (c) A subphrenic abscess may be secondary to pylephlebitis set up by appendicitis; such a pylephlebitic abscess on the convexity of the liver may rupture and produce an abscess between the liver and diaphragm. (d) A residual abscess, the result of widespread peritonitis due to appendicitis, may form over the right lobe of the liver or around the spleen.

2. Suppuration in the liver frequently sets up a non-gaseous subphrenic abscess. Collections of pus in the substance of the liver, such as tropical abscess, a suppurating hydatid cyst, multiple abscesses due to pylephlebitis or to cholangitis, whether associated with gall-stones or not, may by extension set up an abscess between the convexity of the organ and the diaphragm, or between the layers of the coronary ligament. Operations on the liver or bile ducts may give rise to leakage of infective material from inflamed areas in the liver. As rare causes of a subphrenic abscess, attention may be called to leakage of a tuberculous or of an actinomycotic abscess near the surface of the liver, or even of a softened and infected gumma in that situation.

3. An abscess of the spleen, by leaking or rupture, readily sets up a subphrenic abscess. Trauma, by giving rise to hemorrhage from or around the spleen, may be the first step in the production of a subphrenic abscess on the left side.

<sup>1</sup> *Medical News*, New York, 1903, lxxxii, 147.

4. Although a localized abscess following perforation of a gastric ulcer nearly always contains gas, a very minute perforation, such as that produced by a pin, may set up a simple abscess. It is possible that microorganisms may pass through the floor of an ulcer, and that suppuration may occur without any gross perforation. Among 27 non-gaseous subphrenic abscesses at St. George's Hospital, 2 were associated with a non-perforated gastric ulcer. A non-gaseous abscess occurs in about 3 per cent. of all cases of gastric carcinoma, but the resulting abscess is usually not in actual contact with the diaphragm, and therefore rather comes within the category of perigastric abscess. The writer has seen a subphrenic abscess in connection with breaking down carcinomatous lymphatic glands close to the cardiac orifice of the stomach, the primary growth being in the lower end of the œsophagus.

5. Perforation of a duodenal ulcer usually floods the peritoneal cavity and sets up general peritonitis, but there are two ways in which it may set up a localized abscess (Maynard Smith<sup>1</sup>): (a) Perforation of the serous surface of the duodenum may be followed by the escape of a moderate amount of fluid into the right kidney pouch, and by the formation of an extensive abscess. (b) Perforation of the duodenum behind the peritoneum may give rise to a localized abscess. Osler estimates that 6 per cent. of subphrenic abscesses are due to duodenal ulcer. In his digest of 184 cases of duodenal ulcer, Cullen<sup>2</sup> finds that in 10 per cent. an abscess forms outside the duodenum, and that ultimately the ulcer opens into the abscess. In most exceptional instances a left-sided subphrenic abscess is due to a duodenal ulcer (Rolleston,<sup>3</sup> Box<sup>4</sup>).

6. A pericolic abscess may, but often does not, lie in contact with the diaphragm. Pericolic abscesses at the hepatic or splenic flexures of the colon will necessarily be those likely to become subphrenic.

7. Suppuration in or around the pancreas may spread so as to lie immediately under the diaphragm.

8. Suppuration in connection with the Fallopian tubes may, like an appendicular abscess in the pelvis, track up along the colon and give rise to a subphrenic abscess.

9. Retroperitoneal suppuration starting from the kidneys, and from tuberculous disease of the spine or even of the ribs, must be mentioned, since the abscess may be subphrenic, but the clinical picture is usually different from that of the other simple subphrenic abscesses.

10. It is sometimes stated that an empyema, other forms of intrathoracic suppuration, or even pneumonia, may lead to a subphrenic abscess. Tuberculous ostitis of the dorsal spine is commonly followed by a psoas abscess, but subphrenic abscess undoubtedly due to intrathoracic causes is extremely rare; in 448 collected cases there were 18 in which a subphrenic abscess was due to intrathoracic infection (Archibald<sup>5</sup>). In any given instance, therefore, it is more probable that the

<sup>1</sup> *Lancet*, London, 1906, i, 895.

<sup>2</sup> *Scottish Med. and Surg. Jour.*, Edinburgh, 1897, i, 643.

<sup>3</sup> *Brit. Med. Jour.*, 1912, i, 423.

<sup>4</sup> *Ibid.*, 1912, i, 889.

<sup>5</sup> *Ibid.*, 1906, i, 1148.

subphrenic abscess was the primary condition, but remained latent or was undetected for a time. Exploration of an empyema, however, may convey infection into the subphrenic space and so start an abscess below the diaphragm. In very rare cases suppuration in the posterior mediastinum, due to œsophageal ulceration, may track down and produce a subphrenic abscess. The infrequency with which infection spreads from the thorax to the abdomen is in marked contrast to the ease with which infection passes by the lymphatics from the peritoneum to the pleura. In 62 cases of streptococcic empyema, 14 spread from the abdomen (Pitt<sup>1</sup>).

11. In some instances the focus from which a subphrenic abscess arose cannot be found. Possibly a minute traumatic rupture of a solid organ allowing hemorrhage to occur, or perforation of some part of the alimentary tract by a small foreign body may be the real cause in some cases. Trauma may appear to be the only antecedent event.

*Age and Sex.* In 27 non-gaseous subphrenic abscesses at St. George's Hospital the average age was thirty-five years, being thirty-eight in 14 males and thirty-one in 13 females; in this series the incidence in the sexes was practically equal.

**Morbid Anatomy.**—Since a simple subphrenic abscess is in the majority of cases due to disease of the appendix or liver, it is much more often met with on the right than on the left side. It may be intraperitoneal or extraperitoneal, but is more commonly intraperitoneal. In 73 cases of subphrenic abscess due to appendicitis collected by Elsberg,<sup>2</sup> 35, or 48 per cent., were intraperitoneal; 20, or 27 per cent., extraperitoneal; and in 18, or 25 per cent., the position was not determined. Retroperitoneal abscesses due to lesions of the spine or kidney are more allied to lumbar than to subphrenic abscesses. From a pathological point of view the greater cavity of the peritoneum is divisible into two parts: (a) Above the transverse mesocolon and omentum, supra-omental or supramesocolic; and (b) below the transverse mesocolon and omentum, or infra-omental. Intraperitoneal subphrenic abscesses occur in the supra-omental division of the greater sac. The anatomical boundaries of subphrenic abscesses vary according to the position of the abscess, and are further modified by the presence of old adhesions. The following descriptions may be regarded as applying both to simple and to gas-containing subphrenic abscesses.

The anatomical boundaries of subphrenic abscesses have been described by Box and Eccles,<sup>3</sup> and Carnot.<sup>4</sup> Barnard<sup>5</sup> described six forms of subphrenic abscess corresponding to six areas on the under surface of the diaphragm, four intraperitoneal and two extraperitoneal; the four intraperitoneal forms of subphrenic abscess are named (1) right anterior, (2) right posterior, (3) left anterior, and (4) left posterior; the areas on the diaphragm corresponding to these are defined and separated from

<sup>1</sup> *Clinical Journal*, London, 1907, xxxi, 81.

<sup>2</sup> *Ann. Surg.*, 1901, xxxiv, 729.

<sup>3</sup> *Clinical Applied Anatomy*, 1906.

<sup>4</sup> *Sem. méd.*, Paris, 1906, xxvi, 85.

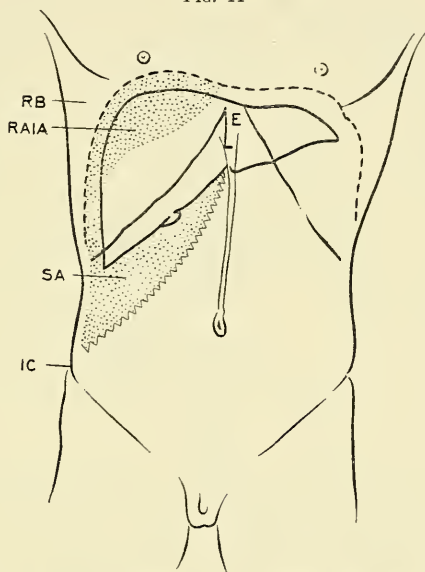
<sup>5</sup> *Brit. Med. Jour.*, 1908, i, 371.



each other by the cruciform arrangement of the peritoneal ligaments—the falciform, coronary, and right and left lateral—of the liver. The two extrahepatic subphrenic abscesses are (5) the right and (6) the left.

1. The right anterior subphrenic abscess is between the diaphragm and the convexity of the liver, and is bounded to the left by the falciform ligament, behind by the right lateral ligament of the liver, and in front by adhesions which vary somewhat in position; toward the right it communicates, unless shut off by adhesions, with the subhepatic or right kidney-pouch (Rutherford Morison), in which the right posterior intraperitoneal subphrenic abscess is situated.

FIG. 11



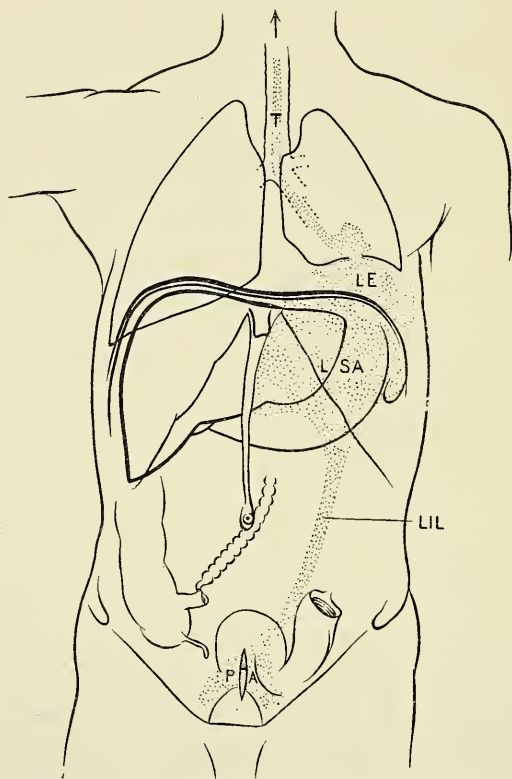
The abdominal signs when a right anterior intraperitoneal subphrenic abscess (RAIA) is combined with a subhepatic abscess (SA) in the right kidney-pouch as often occurs in appendicular cases. The former (RAIA) produces signs of compression and inflammation at the base of the right lung (RB). The latter (SA) produces a triangular swelling below the liver margin, limited toward the abdomen by a band of tender rigid adhesions running from the ensiform cartilage (E) back into the right loin, usually as low as the iliac crest, IC. Pus or gas may be found in contact with the abdominal wall within the triangle. This and the two following figures are reproduced from Barnard's paper in the *Brit. Med. Jour.*, 1908, i, 371.

2. This right kidney-pouch may contain a pint of fluid before its contents run over into the remainder of the peritoneal cavity. Its boundaries are the right lobe of the liver above and in front, the hepatic flexure of the colon below, the parietal peritoneum of the lumbar region externally, the descending duodenum and lumbar spine internally, and the right kidney posteriorly. An abscess in this position commonly tracks up over the convexity of the liver into the right anterior subphrenic intraperitoneal space, and it may pass through the foramen of Winslow into the lesser sac of the peritoneum.

3. The left anterior intraperitoneal abscess (Barnard) is in the dome of the stomach chamber and is in relation with the stomach and the

spleen, or perigastric and perisplenic, and occupies a pouch which corresponds to the right kidney-pouch (Box and Eccles) (Fig. 12). The phrenicocolic peritoneal ligament, binding the splenic flexure of the colon to the diaphragm and forming the suspensory ligament of the spleen, constitutes the lower margin of this pouch and and, so to speak, dams up fluid in this peritoneal recess. The boundaries of left-sided intraperitoneal subphrenic abscesses are subject to some variation and Barnard's

FIG. 12



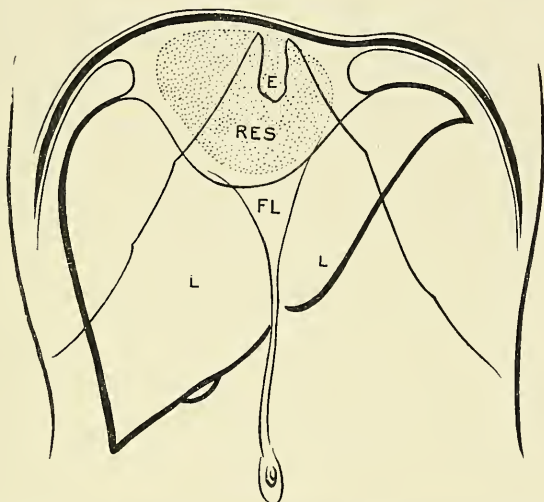
Left anterior intraperitoneal subphrenic abscess (*LSA*) due to infection conveyed from pelvic appendicular abscess (*PA*) along (*LIL*) the left internal lumbar fossa (Barnard), or left internal paracolic groove (Jenkins and Maynard Smith). It has set up left-sided empyema (*LE*) which has burst into the trachea. (Barnard.)

description is not followed here. Usually the abscess is between the left lobe of the liver, the diaphragm, the cardiac end of the stomach, and the spleen; the abscess passes deeply toward the back of the abdomen in relation to the spleen, and has the left kidney, adrenal, and tail of the pancreas behind. The spleen may lie in the middle of the abscess, and the abscess is often tortuous and irregular in outline as it passes around the margins of liver and spleen. In some cases the abscess is mainly to the left of the spleen, between it and the diaphragm; according

to Hunt<sup>1</sup> this position of the abscess follows perforation of an ulcer on the posterior wall of the stomach. The abscess may also occupy the space between the diaphragm and the left lobe of the liver, passing downward and to the right, under the liver, and in front of the stomach. Such an abscess is usually the result of suppuration in the left lobe of the liver or in connection with the anterior surface of the stomach.

4. An abscess confined to the lesser sac of the peritoneum is rare; it constitutes Barnard's left posterior intraperitoneal abscess.

FIG. 13



The signs of a right extraperitoneal subphrenic abscess (*RES*) pointing in the epigastrium below the ensiform process (*E*) and having separated the layers of the falciform ligament (*FL*) so that the abscess may be opened extraperitoneally. The liver is pushed down. (Barnard.)

The median boundary of abscesses in contact with the under surface of the diaphragm is formed by the falciform ligament of the liver, which may be displaced by the pressure of the abscess, but is hardly ever perforated. It is extremely rare to find suppuration on both sides of the falciform ligament at the same time; but suppuration starting in the pelvis may track up in the paracolic grooves on both sides of the abdomen, and so give rise to abscesses in contact with the hepatic and splenic flexures of the colon.

5. The right extrahepatic abscess is in the uncovered space between the layers of the coronary ligament of the liver, and is closely allied to if not the same as the suprahepatic abscess described by Cantlie.<sup>2</sup> It is nearly always due to intrahepatic suppuration.

6. The left extraperitoneal abscess (Barnard) is near the left kidney and is rare. Barnard finds that the right anterior and left anterior intraperitoneal abscesses, due in the main to appendicitis and to

<sup>1</sup> *Transactions of the Medical Society, London, 1905, xxviii, 75.*

<sup>2</sup> *Brit. Med. Jour., 1899, ii, 646.*



perforated gastric ulcer respectively, are the commonest; next in order of frequency comes the right extraperitoneal abscess.

The walls of the abscess are formed of shaggy fibrin, the diaphragm, surface of the liver, intestines, and so forth, being infiltrated for a considerable distance with organizing granulation tissue. The size of the abscess varies very considerably in different cases; it may be as small as a man's fist or larger than a child's head, and contain several pints of pus. In cases of appendicular origin the pus is often putrid.

A subphrenic abscess readily sets up inflammation of the adjacent pleura and leads to an effusion which may be serous and sterile, fibrinous or purulent. This occurs in about half the cases of subphrenic abscess. Like an abscess in the liver, it may perforate the diaphragm and open into the pleura, leading to empyema, into the lung, thus setting up gangrenous pneumonia, multiple abscesses, and extensive disorganization of the lower lobe, or in very rare cases it may open into the pericardium. In Lang's<sup>1</sup> 173 cases of subphrenic abscess the diaphragm was perforated in 67, and in Martinet's<sup>2</sup> 138 cases in 33; both these series include gaseous as well as non-gaseous abscesses. Intraperitoneal abscesses are less prone than extraperitoneal abscesses to perforate the diaphragm. The pus in the empyema may be extremely offensive; Dieulafoy<sup>3</sup> reported cases in which a non-gaseous subphrenic abscess of appendicular origin gave rise to a pyopneumothorax, the gas being due to bacterial activity and not to a communication with the lung or any of the hollow viscera. As the result of the rupture into the lung of a subphrenic abscess, set up by intrahepatic suppuration, a bronchobiliary fistula, with copious bile-stained expectoration, may be established. Rupture externally or into the hollow viscera—the stomach or colon—is rare. Inflammation may extend to the portal vein and set up adhesive or, as a later stage, suppurative pylephlebitis. Rupture into the peritoneal cavity is usually fatal. It occurred once only among 23 cases of spontaneous rupture of a subphrenic abscess (Barnard).

**Bacteriology.**—The colon bacillus is commonly present; streptococci, staphylococci, pneumococci, *Bacillus pyocyaneus*, *B. typhosus*, actinomyces, and *Micrococcus melitensis* have also been found.

**Symptoms.**—These are somewhat obscure and vary to some extent according to the origin and the position of the abscess. Thus an abscess between the convexity of the liver and the diaphragm will resemble an intrahepatic abscess, while a purulent collection in the lesser sac of the peritoneum (bursa omentalis) will present features like those of a pancreatic cyst. In fact, subphrenic abscesses in these two positions are, from a clinical point of view, closely bound up with diseases of the liver and pancreas respectively.

The onset of symptoms is usually gradual, and it may be difficult to distinguish between those due to the primary disease, such as appendicitis or calculous cholangitis, and those depending on pus formation under the diaphragm. After an operation for an appendix abscess,

<sup>1</sup> *Thesis*, Moscow, 1895.

<sup>2</sup> *Thèse de Paris*, 1898.

<sup>3</sup> *Clinique médicale de l'Hôtel-Dieu de Paris*, 1901–1902, iv, 105.

continued fever, diarrhœa, and quick pulse may persist, and after some time signs at the base of the right lung suggest that an abscess has formed under the diaphragm. In some instances the thoracic manifestations, such as pleurisy, are the first to attract attention. This gradual onset contrasts with the sudden pain which marks perforation of the stomach in the majority of the cases of subphrenic pyopneumothorax. In some instances there is a sudden onset with a rigor.

Physical signs may be absent or so slight as to be easily overlooked, and are less obvious than in gaseous subphrenic abscess. From the point of view of physical signs, simple subphrenic abscesses have been divided into two groups: (1) those in which the thorax is mainly affected, and (2) those in which the signs are mainly abdominal.

1. Since a subphrenic abscess is usually nearer the spinal attachment of the diaphragm than the epigastrium, the signs are chiefly found posteriorly, and are more thoracic than abdominal. There is dulness at the base of one, usually the right, lung, which slowly increases upward toward the inferior angle of the scapula; there may be bronchial breathing from compression of the lung, a friction rub from concomitant pleurisy, or, from pleural effusion, absence of breath sounds. The physical signs, therefore, resemble those of pleural effusion. Examination with the *x*-rays may be of the greatest use by showing that the diaphragm on the affected side is pushed upward by a dark area, and that the excursions of the diaphragm are restricted or absent.

2. In some cases, in which the manifestations are abdominal, a subphrenic abscess may pass forward, present anteriorly below the costal margin, and give rise to tenderness, fulness, and prominence of the hypochondrium and epigastrium, restricted movement of the ribs, muscular resistance, and a more or less definitely palpable tumor, which is dull on percussion. The dulness is constant and does not alter when the patient's position is changed. Under an anesthetic the muscular rigidity passes off, and the intestine may pass in front of the abscess cavity and so lead to resonance where there was previously dulness on percussion (Godlee<sup>1</sup>). As the abscess approaches the surface the skin may become œdematous and red, and fluctuation may be obtained. The manipulation necessary to elicit this sign is, however, not without risk of producing rupture into the general peritoneal cavity. Pain is usually not a severe symptom, and, as a rule, is pleuritic and transient; it may be felt at the angle of the scapula. The temperature is nearly always raised and may show the oscillations of suppuration, but in a few instances fever is absent. The pulse is quick, the respirations are often irregular, painful, and rapid, especially when the thorax is much invaded; cough is exceptional. Leukocytosis up to 30,000 may be present. The appetite is poor, wasting is considerable, and there may be frequent perspirations, especially at night, and considerable secondary anemia. When clubbing of the fingers occurs in a case thought to be one of subphrenic abscess the lesion will probably turn out to be above the diaphragm (Acland<sup>2</sup>). With continued temperature and progressive loss

<sup>1</sup> *Lancet*, London, 1905, i, 482.

<sup>2</sup> *System of Medicine* (Albutt and Rolleston), 1907, iii, 1007.

of strength the patient steadily goes down hill unless the abscess be freely drained. The abscess may extend and open into the pleura, lung, bronchus, into the peritoneum, one of the abdominal viscera, or even externally through the ribs or at the umbilicus. In exceptional instances the abscess has burst into the pericardium, or has tracked up into the neck (Cullen). Pulmonary embolism may result from thrombosis of branches of the inferior vena cava. Death usually results from exhaustion. The duration of the disease, if it be left to run its natural course, is from two to three months.

**Diagnosis.**—When there is no antecedent condition, such as appendicitis or suppuration elsewhere in the abdomen, the existence of a subphrenic abscess may not be suspected unless there be a palpable swelling. On the other hand, when after operation on an appendix abscess or on the gall-bladder or biliary passages, the patient's general condition still suggests suppuration, careful examination of the bases of the lungs by percussion, auscultation, and the *x*-rays may show signs compatible with a small abscess or effusion. The affected area should then, as Barnard directs, be systematically explored with a syringe, the needle of which is at least three inches long and sufficiently large to enable thick pus to be withdrawn. The patient is fully prepared for operation and anesthetized, and the needle is passed deeply—for three inches—into the 10th intercostal space in the scapular line, and then, if no pus be found, into the 9th, 8th, 7th, and 6th spaces in turn; if necessary, the same spaces in the midaxillary line are explored from below upward. When a subphrenic abscess presents under the anterior abdominal wall the exploring syringe should not be used.

**Differential Diagnosis.**—The chief difficulty in distinguishing between subphrenic abscess and other intra-abdominal conditions on the right side is in deciding whether the collection of pus is inside the right lobe of the liver or between it and the diaphragm. Enlargement of the liver downward is in favor of intrahepatic suppuration, but in many instances it is impossible to come to a positive conclusion, and, indeed, a subphrenic abscess is often due to leakage of an intrahepatic focus of suppuration. A subphrenic abscess on the left side presenting as a palpable swelling must be distinguished from soft tumors, innocent, such as perirenal lipomas, or malignant, such as retroperitoneal sarcomas. The raised temperature and signs of septic absorption should be taken into account in forming an opinion, but a swelling in the left hypochondrium of rather sudden onset, accompanied by pain and a raised temperature, has turned out to be a retroperitoneal sarcoma. In some instances a large, false abdominal aneurism on the left side does not pulsate and no bruit is audible over it; the diagnosis may then be very difficult (T. Holmes<sup>1</sup>). Persistent leukocytosis is in favor of abscess, but a posthemorrhagic leukocytosis may occur in aneurism.

The main difficulty, however, is not in distinguishing between subphrenic abscess and other abdominal conditions, but between subphrenic abscess on the one hand and an empyema or pleural effusion

<sup>1</sup> *St. George's Hospital Reports*, 1875, vii, 173.



on the other. It has happened that when an abscess diagnosed as an empyema is drained, particles of food are found in the discharge, and for the first time indicate the underlying cause. In a simple subphrenic abscess on the right side the liver is more depressed, the breath sounds less cut off at the base of the lung behind, and the constitutional symptoms are more marked in comparison with the thoracic dulness than in an empyema. Skiagraphy shows that the diaphragm is pushed up instead of being depressed.

The question whether the collection is above or below the diaphragm is often rendered more difficult by the not infrequent presence of a pleural effusion secondary to the suppurative process under the diaphragm. When a pleural effusion and a subphrenic abscess are both present the latter is extremely likely to be overlooked. This combination, if suspected, may be recognized by the withdrawal by the exploring syringe of pus from one interspace and serous fluid from one above it. This sign, however, is not infallible, for in rare cases a loculated pleural effusion may contain serum in one loculus and pus in another.

Brief reference may be made to two signs which have been employed in order to decide whether a given collection of fluid is above or below the diaphragm. If the aspirating needle is introduced into a cavity above the diaphragm no movement of the needle occurs on respiration; if the needle passes through the diaphragm the extrathoracic part of of the needle moves upward in inspiration and downward in expiration; this is Fürbringer's sign. The second sign is Pfühl's; when the needle enters a subphrenic abscess the manometric pressure and the outflow of pus are greater during inspiration and less during expiration, while the reverse holds good in the case of an empyema. These two signs depend on the normal excursions of the diaphragm being maintained, but this does not always hold good; for example, a pleural effusion may paralyze the diaphragm and so lead to mimicry of the condition in a subphrenic abscess. Further puncture of the diaphragm may convey infection from the abdomen to the thorax, or *vice versa*, and is therefore not devoid of danger.

**Prognosis** in non-gaseous subphrenic abscess depends on the condition being recognized and promptly treated by exploration and thorough drainage. If the abscess be not opened the case will almost certainly terminate fatally; further, it is most important that the abscess should be opened before it has extended into the lung or given rise to septicemia. Even when opened there is a risk that some loculus of the abscess may not drain properly. The difficulty in diagnosing and, when the existence of the abscess is suspected, in accurately locating the abscess makes the prognosis grave. A subphrenic abscess may be opened successfully, but an empyema may be overlooked and subsequently prove fatal.

Most of the available statistics contain both simple and gas-containing abscesses, so that it is difficult to compare the mortality of the two forms. In Elsberg's 73 cases of subphrenic abscess (15 per cent. of which were gaseous) due to appendicitis, 51 were operated upon, with recovery in 40, or 78.4 per cent., while of 22 not operated upon 18, or 82 per cent.

died. Out of Barnard's 76 cases, 36, or 47.4 per cent., died; 12 cases were only recognized after death and were not operated upon. Of the remaining 64 the mortality was 37.5 per cent., but after making allowance for imperfect diagnosis and treatment, Barnard concludes that the mortality should be 16 per cent.

**Treatment** is purely surgical.

**Subphrenic Pyopneumothorax.**—The peculiarity of this form of subphrenic abscess is that at the bedside it imitates an ordinary pneumothorax or pyopneumothorax. The existence of a gaseous abscess underneath the diaphragm was first diagnosed during life as a logical deduction from the physical signs by G. H. Barlow<sup>1</sup> as far back as 1845, but it was not until Leyden's<sup>2</sup> article, in 1880, that it became generally recognized and the subject of numerous papers. It seems that since perforated gastric ulcers have been treated by immediate operation this form of subphrenic abscess has become less common.

**Etiology.**—The causes of a gaseous subphrenic abscess are less numerous than those of a simple subphrenic abscess. Perforation of a gastric ulcer is the most important cause. In the sixty years, 1846 to 1906, there were about 26,000 autopsies at St. George's Hospital, among which Wahby found 32 gaseous subphrenic abscesses, 25 (21 females, 4 males) of which, or 78.1 per cent., were due to perforated gastric ulcer. In order that the resulting peritonitis should be localized, certain conditions are necessary; thus preëxisting adhesions which prevent the gastric contents from spreading widely over the peritoneum are of great importance. It is, however, highly probable that in certain circumstances perforation of the stomach may lead to a localized abscess even in the absence of these adhesions; the occurrence of perforation in a stomach containing but little food, in a patient in the supine position, so that only a small quantity of the gastric contents escapes and does not travel far into the peritoneal cavity, and then mainly into the upper part, gives a combination of circumstances in which the inflammatory process may become circumscribed instead of generalized. The position of the perforation is another factor of importance: if on the posterior surface, a localized abscess is likely to follow, while if it is on the anterior surface, general infection of the peritoneum is apt to occur. Perforation of an ulcer close to the pylorus may lead to a localized abscess in the right kidney-pouch. Perforation of the stomach due to carcinoma is a rare cause of a gaseous abscess.

Perforation of a duodenal ulcer usually gives rise to general peritonitis, but in a small minority of the cases a subphrenic pyopneumothorax on the right side results. As long ago as 1862, Bouchard recorded a case. Out of 32 gaseous subphrenic abscesses at St. George's Hospital, 6 (3 males, 3 females), or 19 per cent., were due to perforation of a duodenal ulcer.

An abscess in the neighborhood of the stomach or duodenum has in rare instances perforated (exogenous ulceration) into the alimentary

<sup>1</sup> *London Medical Gazette*, 1845, i, 13.

<sup>2</sup> *Zeil. f. klin. Med.*, 1880, i, 320.

canal, with the result that a gaseous subphrenic abscess is produced. A suppurating hydatid cyst of the liver may rupture into the alimentary canal and become gaseous, but this condition, of which Dévé<sup>1</sup> has collected 7 examples, is not the same as an ordinary subphrenic pyopneumothorax. A suppurating hydatid of the liver, from infection with anaërobic organisms, may contain gas, and in rare instances, by rupturing into the space between the liver and the diaphragm, may produce a subphrenic pyopneumothorax on the right or left side, according to the position of the cyst in the right or left lobe of the liver. In Maydl's<sup>2</sup> collection of 179 cases of subphrenic abscess there were 3 of gaseous subphrenic abscess due to hydatid cysts of the liver. Perforation of an ulcer in the colon very seldom produces a gaseous abscess.

An appendicular abscess, although usually simple, may be gaseous; this was so in 15 per cent. of the 73 cases of subphrenic abscess due to appendicular infection analyzed by Elsberg.<sup>3</sup> The presence of gas in these abscesses was at first considered to be due to secondary communication with some air-containing viscus, but it is, in many instances at least, of bacterial origin.

**Morbid Anatomy.**—The situation and boundaries of subphrenic abscesses have been described. In contrast to simple subphrenic abscesses, which are much commoner on the right side, gas-containing subphrenic abscesses are in the great majority of cases on the left side. This is due to the preponderating influence of perforated gastric ulcers as the causal factor.

The diaphragm is pushed up so as greatly to encroach on the cavity of the thorax. The perforation in the stomach or duodenum is usually open, but in some instances becomes closed with fibrin. The size of the cavity may vary considerably; sometimes these abscesses are very large, and have been known to contain in addition to gas a quart of purulent fluid with an admixture of gastric contents of an extremely offensive character. The abscess may erode the substance of the spleen. Perforation into the general cavity of the peritoneum occurs in a few cases. The inflammatory process readily spreads through the diaphragm and sets up pleurisy with effusion and collapse of the lower lobe of the lung. The effusion is usually serous or serofibrinous, but may be purulent, and in this even the lung may be disorganized by multiple abscesses. Perforation of the diaphragm may be followed by a true pyopneumothorax or, when the lower lobe of the lung is already adherent to the diaphragm, by suppurative destruction of the lung or gangrenous pneumonia; or the abscess may rupture into the bronchi. Pericarditis may be found, but is not so frequent as pericardial friction during life.

**Age and Sex.**—As most cases are due to perforation of a gastric ulcer, the patients are chiefly young women. In the 32 cases at St. George's Hospital the average age was thirty-three years, being thirty years in the 24 females and forty-two years in the 8 males. Vanlair recorded a gaseous subphrenic abscess in a boy six years of age.

<sup>1</sup> *Rev. de chir.*, Paris, 1907, xxxv, 529.

<sup>2</sup> *Ueber subphrenische Abscesse*, 1894, Vienna.

<sup>3</sup> *Annals of Surgery*, 1901, xxxiv, 729.



**Symptoms.**—The onset is usually sudden, with very severe pain, due to perforation of the stomach; in this respect it differs from the simple subphrenic abscesses in which the onset is often insidious. In some cases, however, the leakage from the stomach is quite latent. The patient's history often shows indications of gastric ulcer. The pain, which is agonizing and may be accompanied by collapse, is situated in the upper part of the abdomen, usually on the left side. The onset may be accompanied by vomiting, which may or may not persist afterward; the vomited matters may contain blood and bile. It is important to realize that vomiting may occur after perforation of a gastric ulcer, and that this event does not seriously militate against that accident. Directly after the onset the abdomen becomes extremely tender, so that accurate examination may be impossible at first; as a rule, it rapidly becomes distended, although in men it may be rigidly contracted, tympanitic, and does not move on respiration. The temperature becomes raised, the pulse and respiration rates are rapid, rigors may occur, leukocytosis is present, there is nocturnal sweating, and the patient has the general appearance of suppuration with abdominal pain and some respiratory embarrassment.

The *physical signs* may very closely resemble those of a true pneumothorax or pyopneumothorax. There is a tympanitic note on percussion over an area of distension in the upper part of the abdomen; the altered note extends up into the thorax for a considerable distance, but not to the extreme apex. On the right side the diaphragm may be displaced as high as the second rib, but the presence of the heart prevents the same amount of upward displacement on the left side. The tympanitic note may be mainly behind the sternum. There is dullness posteriorly on the affected side when the patient is lying on his back, and when turned on his side the positions of the dull and tympanitic areas alter as in a pyopneumothorax. A bell or coin percussion note, amphoric breathing, succussion, and metallic tinkling may be heard over the swelling and part of the chest. When the left side is affected the heart is displaced upward, but only slightly to the other side, thus differing from what occurs in a true pneumothorax. When the abscess is on the right side the liver may be greatly displaced downward and be palpable below the umbilicus; the hepatic dullness will then be absent from its normal position. The costal margin is pushed out and the lower intercostal spaces may bulge as in pneumothorax.

Thoracic complications are almost constant. Signs of pleurisy rapidly come on, but in some instances the signs are those of pneumonia of the base of the lung on the corresponding side. The effusion is usually serous at first, but may subsequently become purulent. A pleuropericardial or pericardial friction rub is not uncommon. Secondary parotitis occasionally occurs, and if suppuration supervenes may prove very serious. In rare instances subcutaneous emphysema has appeared.

**Diagnosis.**—The common error is to regard as a pyopneumothorax a gaseous abscess which is below the diaphragm. While the history and mode of onset frequently point to the abdomen rather than to the thorax, the signs suggest a pyopneumothorax from which it can be

most certainly distinguished by a skiagram showing the position of the diaphragm.

The physical signs in favor of a gaseous subphrenic abscess are that the pneumothorax appears to be partial, not universal, as shown by the presence of normal breathing over the upper part and apex of the lung; that the heart's apex is displaced upward and but little to the opposite side; that a bell note and other signs of an air-containing cavity can be obtained well below the limits of the thoracic cavity, for example, below the left costal margin; and that cough and expectoration are late in appearing, or insignificant.

A subphrenic pyopneumothorax is often complicated by a pleural effusion—serous or purulent; the diagnosis of these two concomitant conditions may be greatly aided by the withdrawal of pus and gas from one interspace, and of serum or pus of a different character from a higher interspace. The fluid from a subphrenic abscess comes out more freely during inspiration, while in a pleural effusion its exit is accelerated during expiration. It must be remembered, however, that puncture of the chest, although often desirable to determine whether, and if so where, operative procedures should be carried out, may spread infection from the pleura to the peritoneum or *vice versa*.

The diagnosis from a pleural effusion rests on the detection of the signs of a cavity containing fluid and gas, on the changing dullness in a gaseous subphrenic abscess, and on the absence of this change in a pleural effusion (Godlee), on the lateral displacement of the heart in a pleural effusion, and upon its upward displacement in a subphrenic gaseous abscess.

Abdominal distension due to flatulence may be accompanied by disappearance of the normal liver dullness and by a bell note, but the liver cannot be felt to be displaced downward.

A diaphragmatic hernia on the left side which contains the stomach gives rise to signs resembling in many respects those of a pyopneumothorax, but the abdomen falls in instead of being distended, and the heart is pushed over to the right side very much more than in a subphrenic pyopneumothorax. In making a diagnosis the *x*-rays should be employed, and a metal probe passed into the stomach and its position noted.

**Prognosis.**—In subphrenic pyopneumothorax this is always grave, partly because the extension of inflammation to the pleura and lung is a frequent and serious complication, and partly because the large abscess cavity may not close and the patient dies from toxic absorption.

**Treatment** is surgical, and consists in opening and draining the abscess.

### SIMPLE CHRONIC PERITONITIS

This condition may for convenience be divided into (1) circumscribed or localized areas of chronic peritonitis, and (2) diffuse chronic peritonitis. There are necessarily transitional cases in which the chronic peritoneal change is, on the one hand, not sufficiently localized to be included in the first category, and, on the other hand, is far from implicating the

whole of the peritoneal cavity. As a matter of fact, chronic peritonitis is seldom universal and equally well-marked over the entire abdominal cavity. The change may be advanced in the upper part of the abdomen over the liver, spleen, and omentum, and slight in the pelvis.

**Localized Chronic Peritonitis.**—The adhesions due to a past acute peritonitis must be distinguished from the progressive or chronic inflammatory process which alone deserves the name of chronic peritonitis.

The causes of localized chronic peritonitis are numerous. The female genital organs very commonly give rise to chronic pelvic peritonitis which produces dense adhesions around the Fallopian tubes, ovaries, and uterus. The vermiform appendix and the broad ligament may become so matted together that even after death it is extremely difficult to determine in which of these structures the inflammatory process originated. The main cases of chronic perimetritis and pelvic peritonitis are gonococcal and puerperal infections. It is highly probable that hemorrhages from the Fallopian tubes may, as the result of subsequent microbic activity, be responsible for chronic pelvic peritonitis. A chronic gastric or duodenal ulcer may produce progressive localized peritonitis in the immediate vicinity. The contraction of the thickened peritoneum may play a part in producing hour-glass contraction of the stomach, duodenal stenosis, or even stricture of the common bile duct. Appendicitis is an important cause of localized chronic peritonitis in the right iliac fossa. Chronic peritonitis may also be limited to the orifice of hernial sacs, to the surface of the intestines in chronic intussusception, and occasionally, it is said, to the flexures of the colon in chronic stasis. Chronic cholecystitis, especially when associated with gall-stones, may set up very marked local peritonitis which unites the gall-bladder to the neighboring viscera, especially the pylorus.

In hydatid or other cysts, such as ovarian, there may be such thickening of the overlying peritoneum that the condition resembles a lamellar or corneal fibroma. As the result of friction or pressure, chronic capsulitis of the spleen and liver may occur. Localized thickenings, white in color, raised above the surface of the capsule of the spleen, are common in splenomegaly; they are composed of dense white fibrous tissue and are spoken of as lamellar or corneal fibromas. Much less commonly similar masses are found on the surface of the liver.

*Clinically*, the results of localized chronic peritonitis are variable. The lamellar fibromas of the spleen do not give rise to symptoms. Adhesions and indurations around the stomach and flexures of the colon and elsewhere may interfere with the natural movements of the viscera. Thus in the case of the stomach there may be persistent pain after food, or "adhesion dyspepsia;" this is not uncommon in women formerly the subjects of gastric ulcer, and may be thought to be due to a relapse of that disease. As a very rare result of perigastric chronic peritonitis there may be compression of the common bile duct and jaundice. In one example of this, secondary to a chronic ulcer near the pylorus, there was such extensive fibrosis that a tumor, regarded as malignant during life, could be felt. Chronic peritonitis around the gall-bladder may lead to pyloric obstruction and dilatation of the stomach.



Chronic peritonitis around the colon, especially the flexures, may give rise to constipation and pain, especially after defecation; according to the position of the lesion, the condition may imitate appendicitis or malignant disease of the colon. The peritoneal bands in connection with the ascending and transverse colon described by Lane,<sup>1</sup> as the result of intestinal stasis and due to "crystallization of lines of strain" and by Jackson<sup>2</sup> as due to membranous pericolitis, are by others regarded as congenital and not pathological in origin (Flint,<sup>3</sup> Gray and Anderson<sup>4</sup>).

Patients vary much in the way in which they feel such pain; some are martyrs to these painful peritoneal adhesions, while in others—probably in the great majority—there is little or no inconvenience. The adhesions may produce acute intestinal obstruction by kinking and strangulation of the intestine. In some instances the persistent pain suggesting chronic appendicitis may justify laparotomy. Short of this, the treatment should be directed to diet, prevention of constipation, local measures for the relief of pain, and to improvement of the general health.

*Chronic peritonitis involving the sigmoid mesocolon* (perimesosigmoiditis) and the mesentery of the lower part of the ileum (chronic mesenteric peritonitis) was described by Riedel as the result of constipation. But Küss<sup>5</sup> has insisted on the spread of infection from the pelvic organs, especially of females in whom the condition is much commoner than in males, and on the production of stenosis of the sigmoid and rectum by the cicatrizing pericolitis. There is a radiating thickening of the mesocolon which has been regarded as an important factor in the production of volvulus of the sigmoid flexure. The symptoms of pericolic stenosis of the sigmoid and rectum are those of carcinomatous stricture. In one case the dense fibrosis, due to salpingitis, so compressed the ureters as to cause fatal uremia.

Chronic hyperplastic tuberculosis of the intestine usually takes the submucous form, but in a few instances, of which Kidd<sup>6</sup> has collected 6 examples, it is subserous and in at least 3 cases has attacked the sigmoid flexure; it is not improbable that some cases described as subserous fibromas were in reality of this nature.

**Diffuse Chronic Peritonitis.**—Under this heading it is convenient to consider cases which have in common a diffuse peritoneal inflammation of chronic and progressive character, not manifestly due to tuberculosis or new growth. It is sometimes called simple chronic peritonitis to distinguish it from the two forms just mentioned. Chronic proliferative and chronic indurative peritonitis are synonyms sometimes employed, and since ascites is extremely common, the name chronic exudative peritonitis is almost as applicable.

**Etiology.**—There is considerable difference of opinion as to the relative importance of the causal factors. The classification of chronic peritonitis here adopted is: (1) When associated with varying degrees of chronic

<sup>1</sup> *Lancet*, London, 1903, i, 153; *Surg., Gyn., and Obst.*, 1908, vi, 115

<sup>2</sup> *Surg., Gyn., and Obst.*, 1909, viii, 324.

<sup>3</sup> *Johns Hopkins Hosp. Bull.*, Baltimore, 1912, xxiii, 302.

<sup>4</sup> *Lancet*, London, 1913, i, 1300.

<sup>5</sup> *Rev. de chir.*, Paris, 1910, xli, 190, 503, 688.

<sup>6</sup> *Lancet*, London, 1907, i, 9.

inflammation of the pericardium and pleuræ. (2) When associated with arteriosclerosis and granular kidneys. (3) When associated with other conditions. The first two categories are the most important.

1. Simple chronic peritonitis may be combined with inflammatory changes in the pericardium and pleuræ. The association of similar inflammatory changes, whether acute or chronic, in two or more serous cavities has been called polyserositis and polyorrhomenitis.<sup>1</sup> When the condition is chronic it has also been termed multiple progressive hyaloseritis or Concato's disease. The chronic inflammatory changes in the thorax that may be found in association with simple chronic peritonitis vary in extent and intensity; thus there may be chronic indurative mediastinopericarditis with obliteration of both pleuræ, chronic mediastinitis alone, or adherent pericardium. Cases associated with adherent pericardium are the most usual. In some cases of long standing the thickened and adherent pericardium may be calcified; the peritoneal change is then advanced and the liver may be cirrhotic, thus differing from its usual condition of that organ—chronic venous engorgement and fatty change—in chronic peritonitis. It is generally considered that when chronic intrathoracic and peritoneal serositis are associated, the primary focus is more often intrathoracic; but it must be remembered that infection spreads more rapidly from the abdomen to the thorax than *vice versa*.

The original starting-point of the inflammation may thus be on either the upper or under surface of the diaphragm; when there is an adherent pericardium, especially if it be calcified, it is probable that the original focus was in this position. The original lesion may be an acute pericarditis or perihepatitis, or there may be recurrent attacks. But on whichever side it starts it spreads through the diaphragm, the constant movements of which interfere with the natural cure of the morbid process, and so induce the chronic inflammatory process which is most marked on each side of the diaphragm and fades off in the more distant parts of the adjacent serous membranes. The chronic peritonitis is, therefore, most advanced over the liver and spleen.

The pericardial pseudocirrhosis described by Pick<sup>2</sup> is probably allied to this form of chronic peritonitis; Pick, however, believed that a latent adherent pericardium gives rise to circulatory disturbance in the liver, hepatic fibrosis, ascites, and that chronic peritonitis, although it might result from the ascites and repeated tapplings, was a more or less accidental and secondary event. Nicholls<sup>3</sup> and Kelly<sup>4</sup> drew special attention to the association of chronic peritonitis with similar intrathoracic changes.

2. The association with arteriosclerosis and granular (arteriosclerotic) kidneys was insisted on by Hale White,<sup>5</sup> who found it in 19 out of 22 cases of universal perihepatitis and peritonitis, but some observers do not attach much importance to its etiological influence.

<sup>1</sup> Vide F. Taylor, *Brit. Med. Jour.*, 1900, ii, 1693.

<sup>2</sup> *Ztschr. f. klin. Med.*, Berlin, 1896, xxix, 385.

<sup>3</sup> *Studies from the Royal Victoria Hospital*, Montreal, 1902, i, No. 3.

<sup>4</sup> *Amer. Jour. Med. Sci.*, 1903, cxxv, 116.

<sup>5</sup> *Transactions of the Clinical Society of London*, 1888, xxi, 219.

3. Simple chronic peritonitis may occur in combination with various intra-abdominal lesions, or its starting-point may be quite obscure. The associated lesion, such as syphilis of the liver, may reduce the resistance of the peritoneum, or, as in the case of chronic duodenal ulcer or cholecystitis, may provide a local focus for infection. In such cases a widespread chronic inflammatory process results instead of the local reaction which would be expected; this may be compared with the formation of large cheloids after minute injuries, and possibly the excessive reaction may depend on a low resistance, inherent or acquired, of the peritoneum in that individual.

Alcoholism has been regarded as a factor, and would reduce the resistance of the peritoneum and by setting up gastro-intestinal inflammation favor infection. The chronic venous engorgement due to heart and other obstructive diseases would act in much the same manner. The relation of ascites to the chronic peritonitis is usually considered to be that the chronic peritonitis causes the ascites, but it is conceivable that in some circumstances the reverse may hold good; thus, in chronic ascites due to backward pressure of heart disease, repeated tapplings may favor a low form of infection, which is not necessarily introduced from without but may be carried by the blood-stream. In some cases trauma appears to be the exciting factor, and it is quite conceivable that by damaging the viscera it would allow of a low form of infection of the peritoneum. Lastly, no obvious cause may be forthcoming.

**Pathogeny.**—Since the process is evidently a chronic and progressive form of inflammation, it has naturally been surmised that it is the result of infection with microorganisms of a low grade of virulence. Nicholls suggests the *Bacillus tuberculosis*, *B. coli*, and *B. typhosus*. Louis (1825) regarded chronic peritonitis as always tuberculous; in modern times Picchini (1891) argues that subacute and chronic polyorrhomenitis is practically always tuberculous. The recognition in recent years of a special form of tuberculosis, the chronic hyperplastic, which is best known in connection with the ileocecal part of the intestine, suggests that there may be a chronic hyperplastic tuberculous peritonitis which bears the same relation to ordinary tuberculous peritonitis that chronic hyperplastic tuberculosis of the intestine does to ordinary intestinal tuberculosis. As bearing on this view, it may be pointed out that tubercle bacilli are now found in many cases of ascites which do not otherwise suggest peritoneal tuberculosis, and that tuberculosis with fibrotic changes is a not uncommon complication of arteriosclerosis. The last point may help to explain the association of arteriosclerosis and granular kidney with simple chronic peritonitis.

**Morbid Anatomy.**—The appearances vary considerably from the more marked changes of the "iced" organs to a general slight opacity of the peritoneum. In a well-marked case the peritoneum is covered by a thick membrane which resembles a thin layer of cartilage; it is dull white or glistening and pearly in color, and may show pigmentation. This dense layer, especially over solid organs, such as the liver and spleen, for which it forms a firm casing, may show a few depressions like the pitting of sand by rain drops. It is possible that these deficiencies



are the result of rupture of the dense fibrous tissue induced by its own contraction. On the other hand the thick membrane may be locally accentuated in the form of fibrous elevations or nodules, perhaps more often seen on the parietal peritoneum; to this condition the name "peritonitis fibrosa" has been applied; these fibrotic elevations when small may closely resemble miliary tubercles, or when large, nodules of disseminated malignant disease.

The thick membrane, which may be even one-quarter of an inch in depth, can usually be peeled off the liver and spleen, leaving their capsules in a fairly normal condition. From its marked tendency to cicatricial contraction it squeezes the organs and leads to atrophy; in extreme instances these organs may therefore become so atrophied as to be isolated in the abdominal cavity and lose their normal relations. The omentum becomes shortened and rolled up into a firm cord, often in irregular knots, running transversely across the abdomen; in some instances hardly a trace of the omentum is left. In like manner the mesentery becomes retracted, so that the small intestines are anchored to the spine and cannot float in the ascitic fluid, "and, if a hernia has existed, it will sometimes be found to have been completely reduced" (Hodgkin<sup>1</sup>). At the same time there may be such considerable diminution in both the length and diameter of the alimentary canal that the valvulæ conniventes become very closely placed—Prof. W. H. Welch has shown me a specimen in which the longitudinal section of the intestine looked like a comb—and the colon may be no larger than the small intestine. This gives rise to impaired absorption. The condition has been called "peritonitis deformans." Subacute or acute peritonitis may supervene.

Adhesions are often present, but their extent varies greatly. They are more often seen over the solid and relatively fixed organs, since the peristalsis of the intestines interferes with their formation and may rupture them when formed. The remains of adhesions may be seen as filamentous or villous tags on the small intestine, and sometimes resemble miliary tubercles. Adhesions are not uncommon between the liver or spleen and the diaphragm, and may be dense or delicate. Acute strangulation of the intestine due to bands is very rare in this form of chronic peritonitis. When there are sufficient adhesions the ascitic fluid may become encysted, and when the adhesions are so numerous as to obliterate a large area of the peritoneal cavity the fluid effusion may be slight.

The liver and spleen are often described as "iced," or as showing universal chronic capsulitis, and in the case of the liver as "*Zucker-gussleber*" (Curschmann<sup>2</sup>). This condition, also called universal chronic perihepatitis, was formerly regarded as a distinct morbid entity, and many cases of chronic ascites, in reality due to chronic peritonitis, were regarded as the result of chronic perihepatitis, the existence of the more widespread peritoneal change being ignored or regarded as a secondary

<sup>1</sup> *Lectures on the Morbid Anatomy of the Serous and Mucous Membranes*, i, p. 152, London, 1836.

<sup>2</sup> *Deutsche Med. Wchnschr.*, 1884, x, 564.

result of the recurrent ascites and consequent tapplings. From the frequency of ascites in hepatic cirrhosis the liver was considered the important factor in the production of ascites, and disease of its capsule was therefore accepted as a sufficient cause of ascites without any reference to the peritoneal change. The thickness of the membrane varies in different parts; it modifies the shape of the viscera, rounds off the edges, and covers up natural depressions. The gall-bladder may be almost buried, and is usually collapsed, but constriction of the bile duct or portal vein is very rare. In a case at one time under my care prevertebral chronic peritonitis leading to obstruction of the lymphatics and so to elephantiasis was found at the autopsy.<sup>1</sup> The organs usually show chronic venous engorgement, but any considerable extension of fibrosis from the capsule into the substance of the organs is very rare.

*Microscopically* there is extremely dense fibrous tissue laid down in parallel lamellæ, with a few nuclei between. The fibrous tissue is prone to undergo hyaline change, hence the condition has been called hyaloserousitis (Nicholls). The deeper layers of the membrane show bloodvessels with collections of leukocytes and mast cells. Nicholls was unable to find any evidence of fibrin. As the wrinkled peritoneum can be seen underneath, the formation of the membrane is due to organization of exudation, and not to hyperplasia of the peritoneum.

**Clinical Picture.**—The condition most commonly occurs in middle life, but it may be seen in children; the sex incidence is about equal.

The cases may present different manifestations, but the characteristic result is chronic ascites, which requires numerous tapplings and recurs with remarkable persistence. The interval between successive tapplings may diminish in progressive cases so that paracentesis may become necessary every week; more than 100 tapplings may be required. After tapping, the rolled up omentum may be clearly felt running across the abdomen, and is often more distinctly palpable toward the left hypochondrium. The other signs of ascites will be found. The distended abdomen may be almost uniformly dull, since from retraction of the mesentery the small intestines are tethered to the spine and unable to reach the abdominal wall. In rare instances friction is audible. In some cases the fluid is encysted and the abdomen is irregular, so that the diagnosis may be very difficult. Signs of concomitant disease, such as adherent pericardium, valvular disease of the heart, pleural effusion, or renal disease, may be present. The urine is somewhat scanty and may present the characteristics of granular kidney. Jaundice is very rare, and when present is due to some complication.

**Symptoms.**—The onset is, as a rule, gradual; but symptoms may date from a febrile attack, and are usually vague. The first thing noticed is swelling of the abdomen followed by abdominal uneasiness and a sense of fulness and weight, but pain is absent or slight and only brought on by movement. There is naturally some loss of strength, and the muscles are flabby, but emaciation is slow in appearing. Patients may feel well and, except for the abdominal embarrassment, able to be up.

<sup>1</sup> *Brit. Med. Jour.*, 1907, i, 617.

Respiration may be somewhat hampered, constipation is usual and no doubt in part depends on the weakened state of the abdominal muscles, and there may be some flatulency and dyspepsia. Gastro-intestinal hemorrhage does not occur. In the later stages considerable wasting and œdema of the feet supervene. It is noteworthy that œdema of the feet occurs long after ascites has been well established.

The fluid varies to some extent in its characters. Usually it is like serum, of a citron color, and of a specific gravity of 1.015 or more. It may clot and form threads of fibrin or large flocculi. In some instances, in which subacute inflammation has supervened, it becomes turbid. It may be milky or chyliform, and after tapping blood-stained.

**Diagnosis** rests mainly on the presence of chronic and recurrent ascites, for which no other cause is forthcoming. It must be distinguished from other causes of ascites, such as tuberculous and malignant peritonitis and hepatic cirrhosis.

**Prognosis.**—This should be guarded; recovery is rare, but the course is slow, and as many as 100 tapplings may be required. Some cases of the recurrent ascites which are diagnosed as simple chronic peritonitis certainly recover after a number of tapplings. Nicholls found that the duration varied between two and sixteen years. The average duration of Ramsbottom's 9 cases was 624 days.<sup>1</sup> Death is generally due to intercurrent infection, such as pneumonia, but in cases associated with adherent pericardium and chronic mediastinitis it may be due to cardiac failure.

**Treatment** should, in the first instance, be directed to the cause, such as renal disease, heart affections, or syphilis; otherwise it is palliative and symptomatic. No permanent good can be anticipated from laparotomy and the attempt to produce artificial adhesions on the lines of the Talma-Morison operation for the relief of the ascites of portal cirrhosis of the liver. Paracentesis should be performed when required; often this gradually becomes more frequent and may be necessary every week. Injection of adrenin in distilled water into the peritoneal cavity before the cannula is withdrawn is worth a trial.

Diuretics, such as caffeine, may be employed from time to time, and tonics will usually be necessary. Good hygienic conditions and fresh air are desirable. It is not necessary for the patient to remain in bed in the earlier stages. Some relief to the feeling of weight in the distended abdomen may be obtained from the use of a binder or belt.

### TUBERCULOSIS OF THE PERITONEUM AND TUBERCULOUS PERITONITIS

The ordinary clinical heading of tuberculous peritonitis covers cases with somewhat different morbid lesions; thus, although tuberculous inflammation confined to the peritoneum is, strictly speaking, all that is implied, it is customary to include cases having in addition tuberculous

<sup>1</sup> *Medical Chronicle*, Manchester, 1906, xlv, 7.



ulcers of the intestine and tuberculosis of the intra-abdominal lymphatic glands, since these conditions are commonly combined and often cannot be separated during life.

The incidence of peritoneal infection in tuberculosis has been differently estimated. In 531 cases of pulmonary tuberculosis examined after death at the Brompton Hospital, there was tuberculous peritonitis in 22, or 4.1 per cent. (Fowler and Godlee<sup>1</sup>). In 197 cases of tuberculosis at the Boston City Hospital the peritoneum was infected in 14, or 7.1 per cent. (Bottomley<sup>2</sup>). In 1393 cases of tuberculosis at Breslau there was tuberculous peritonitis in 226, or 16.2 per cent. (Borschke<sup>3</sup>). In 300 cases of fatal tuberculosis of various parts of the body at St. George's Hospital the peritoneum was affected in 56, or 18.6 per cent.

**Etiology.**—**Age.**—The disease may occur at any period of life, but it is rare in babies and in old age. Osler records a patient aged eighty-two years, while among 163 cases tabulated by Morley Fletcher,<sup>4</sup> eight were under one year. It is most frequent between twenty and forty years of age. The belief that the disease is commoner in children is probably the result of confusion between chronic intestinal disturbance with a distended abdomen, formerly spoken of as “tabes mesenterica,” and true peritoneal tuberculosis. In 306 cases of tuberculous peritonitis under the age of fifteen, nearly half were between the ages of three and seven years (Faludi<sup>5</sup>).

**Sex.**—In children the sex incidence is equal (Faludi, Morley Fletcher). In adults there is a marked divergence between statistics obtained from postmortem records and those of operation. Postmortem records show that it is more frequent in males; in König's 107 cases, 89 were males. In operation cases females are greatly in excess; this depends on the frequency with which tuberculosis of the Fallopian tubes serves as the starting-point for peritoneal infection.

**Disposing Factors.**—Cirrhosis of the liver shows a decided tendency to be complicated by peritoneal tuberculosis; thus in 584 cases of hepatic cirrhosis, tuberculous peritonitis occurred in 53, or 9 per cent. No doubt concomitant or antecedent alcoholism favors the incidence of tuberculosis generally, but the catarrh of the intestine and the portal obstruction probably play a part in localizing the infection. Injury has, in some cases, preceded the onset of symptoms. Pregnancy, according to H. Kelly,<sup>6</sup> has a definite causal relation to tuberculous peritonitis; in 28 per cent. of his cases the illness was dated from childbirth or a miscarriage. Heredity would naturally be expected to be of some importance in the incidence of tuberculous peritonitis, but in 25 cases investigated by Bottomley there was a history of tuberculosis in 2 only.

**Bacteriology.**—The bovine form of the tubercle bacillus was found by the English Commission on Tuberculosis (1911) in 14 out of 29 cases, and by the German Commission in 63 per cent. of the cases of abdominal

<sup>1</sup> *Diseases of the Lungs*, p. 358, London, 1898.

<sup>2</sup> *Medical and Surgical Report*, Boston City Hospital, 1900, p. 118.

<sup>3</sup> *Virchows Archiv*, 1892, cxxvii, 121.

<sup>4</sup> *Diseases of Children* (Garrod, Batten, Thursfield), p. 242, 1913, London.

<sup>5</sup> *Jahr. f. Kinderh.*, 1905, lxii, 304.

<sup>6</sup> *Operative Gynecology*, 1906, ii, 237.

tuberculosis investigated. In 71 cases in New York 44, or 62 per cent., were bovine; there were 12 adults with bovine tuberculosis in 3, or 25 per cent.; and 41 of 59 children, 69 per cent. of whom were bovine (Hess<sup>1</sup>).

Tubercle bacilli are comparatively seldom found in the peritoneal effusion by ordinary microscopic examination. Jousset's method of inocopy is, however, more successful in leading to their detection. This scarcity of bacilli in the fluid, also seen in tuberculous pleural effusion, is thought to depend on adhesion of the bacilli to the serous membrane. Injection of the ascitic fluid into guinea-pigs proves that bacilli are present.

**Paths of Infection.**—In generalized tuberculosis the miliary tubercles seen on the peritoneum are due to hemic infection, the bacilli reaching the peritoneum by the bloodvessels, but in these cases the peritoneum merely shares in the universal outburst of tubercles and is seldom inflamed. Tuberculous infection usually reaches the peritoneum through the lymphatics. The bacilli may be conveyed from the intestine and vermiform appendix, the lymphatic glands, the pleuræ, the suprarenals, prostate, vesiculæ seminales, and the testes.

It is remarkable how often tuberculous ulceration of the intestine secondary to pulmonary tuberculosis is seen without diffuse tuberculous peritonitis. Thus, among 382 fatal cases of pulmonary tuberculosis at the Brompton Hospital, London, tuberculous ulcers were present in the intestine in 296, or 77.5 per cent., while tuberculous peritonitis occurred in 15 only, or 4 per cent. (Fowler and Godlee). The occurrence of tuberculous peritonitis secondary to primary intestinal tuberculosis is variously estimated. German statistics are to the effect that primary intestinal tuberculosis even in children is very rare, and it is therefore not surprising that among Borschke's 226 cases of tuberculous peritonitis not a single one was secondary to primary intestinal tuberculosis. British statistics give a percentage of primary intestinal tuberculosis in children ranging up to 28.1 per cent. of the cases of tuberculosis (Shennan<sup>2</sup>) and averaging 19 per cent. as against 4 per cent. in Germany and 3 (Harbitz<sup>3</sup>) to 1.3 (Hess) per cent. in the United States. In women tuberculous disease of the Fallopian tubes is a prolific source of tuberculous peritonitis. Primary tuberculosis of the peritoneum, in which there is no tuberculous focus elsewhere in the body, and in which the path by which bacilli have got into the peritoneum is not obvious, is rare. Borschke's series of 226 cases contained only 2.

**Morbid Anatomy.**—A few words may first be devoted to localized tuberculosis of the peritoneum. Local tuberculosis is always present in the subserous tissues of tuberculous intestinal ulcers, and occasionally gives rise to localized peritonitis, as shown by tags of adhesions. There may be localized tuberculosis in the neighborhood of the vermiform appendix or Fallopian tubes. In some instances a hernial sac when operated upon has been found to show localized tuberculosis.

In tuberculous peritonitis the morbid appearances vary considerably.

<sup>1</sup> *Amer. Jour. Med. Sci.*, 1908, cxxxvi, 183.

<sup>2</sup> *Edinburgh Hospital Report*, 1900, vi, 130.

<sup>3</sup> *Journal of Infectious Diseases*, Chicago, 1905, ii, 189.

Strictly speaking, these distinct types of tuberculous peritonitis from a pathological point of view do not exist, for they overlap and one described form may be only the later stage of another. Dupré and Ribierre<sup>1</sup> divide tuberculous peritonitis into (1) acute forms: (a) miliary, part of a generalized tuberculosis with abdominal pain, vomiting and tympanites; (b) miliary tuberculosis of the peritoneum and pleuræ (c) miliary tuberculosis around the cecum resembling appendicitis. (2) Chronic forms—namely, those usually recognized in this country: (a) ascitic, due to miliary tubercles on the peritoneum; (b) caseous, ulcerating, or suppurative; (c) fibrous; (d) localized.

The following method of dividing the anatomical lesions depends on the amount of adhesions present: (1) the ascitic; (2) the loculated, including (a) suppurative or ulcerous and (b) encysted ascites; and (3) obliterative, called chronic fibroid tuberculosis by Osler, fibrous or adhesive by others.

1. In the ascitic form there are few or no adhesions, and the exudation is free in the peritoneum. There is miliary tuberculosis which may be acute, subacute, or chronic. In the more acute forms inflammation of the peritoneum is engrafted on to miliary tuberculosis. The small tubercles vary in size from that of a millet seed downward, are scattered over both layers of the peritoneum, mesenteries, and omentum, and are often more numerous over the diaphragm. In the chronic forms the tubercles are larger, fibrotic, and are often somewhat pigmented; the peritoneum is thickened and the naked-eye appearances may exactly imitate those of malignant disease. The omentum becomes rolled up into a hard mass, the mesentery is shortened from cicatricial contraction so that the intestines become tethered to the spinal column, and from a similar process the intestine becomes shortened in length. These changes resemble those in simple chronic peritonitis.

Pseudotuberculosis is very rare. Dévé<sup>2</sup> described multiple granulomas on the peritoneum enclosing fragments of hydatid membrane and hooklets in cases of rupture of a hydatid cyst; a similar appearance may be due to multiple minute cysts. Pseudotuberculosis due to the ova of a tape-worm has been recorded (Helbing).

2. The loculated or encysted form of peritonitis may be (a) suppurative or ulcerated or (b) ascitic. (a) In the most characteristic and serious form the intestines are matted together by adhesions and enclose collections of serofibrinous, turbid, or purulent exudation. In this form the tubercles increase in size, become confluent masses of caseous material surrounded by fibrin and adhesions, and by softening give rise to suppurating foci among the adherent coils of intestine. There may thus be numbers of intraperitoneal abscesses, the pus of which may erode the walls of the intestine and eventually lead to perforation, and as a result a fecal fistula may form at the umbilicus. Purulent foci may also open into the vagina; in such cases the tubes were probably the original focus of infection. On attempting to unravel the intestines in such a case the bowel is easily torn, and it is sometimes difficult to

<sup>1</sup> *Nouveau traité de médecine* (Brouardel, Gilbert, Thoinet) 1909, xviii, 175.

<sup>2</sup> *Arch. de méd. expér. et. d'anal. path.*, Paris, 1907, xix, 347.



be certain whether perforation was present during life or was made at the necropsy. The adhesions unite all the viscera; the omentum is thickened, contains caseous tubercles, and is usually rolled up into a firm cord. The mesenteric glands are enlarged and caseous; they may soften and give rise to a circumscribed abscess, which in a case seen by the writer imitated a pancreatic cyst.

(b) In the ascitic form of loculated tuberculous peritonitis there is a transition between the ascitic and obliterative forms.

3. The obliterative (chronic fibroid or adhesive) form may follow cure of the ascitic form or develop subacutely. The inflammatory process leads to universal adhesions which unite all the abdominal viscera inextricably to each other and to the abdominal wall; as a result there is no exudation. The tubercles tend to undergo fibrotic changes and show pigmentation. The matted intestines, the rolled up omentum, and masses of caseous glands embedded in adhesions give rise to the tumor-like masses felt through the abdominal wall. In exceptional instances large pendulous caseous masses, resembling "Perlsucht" in animals, have been described in man (Bizzozero,<sup>1</sup> MacCallum<sup>2</sup>).

Tuberculous peritonitis may, as already pointed out, be associated with cirrhosis of the liver; in the vast majority of cases the hepatic change is the older, but some cases of interstitial change due to tuberculous infection of the liver may be secondary to tuberculous peritonitis.

In some cases the serous membranes—pleuræ and peritoneum—seem especially liable to tuberculous infection, and may be notably affected, although there is little evidence of tuberculosis elsewhere in the body. The lymphatic glands in the anterior mediastinum are infiltrated with tubercle as the result of infection from the abdomen.

**Symptoms.**—These vary quite considerably according to the anatomical lesions present. In generalized miliary tuberculosis the infection of the peritoneum may be latent, and, there being no effusion, the peritoneal infection is not suspected during life unless there be abdominal pain or retention of urine and difficulty and pain in micturition. In local peritoneal tuberculosis there may be local pain and tenderness; this may be seen in the neighborhood of the vermiform appendix, and then suggests appendicitis.

The anatomical forms into which diffuse tuberculous peritonitis has been divided may to some extent be correlated with corresponding groups of symptoms and physical signs.

1. In the ascitic form, in which miliary tubercles are scattered over the peritoneum, the characteristic feature is the effusion. The onset is usually gradual and preceded by failing health, loss of appetite, strength, and weight, with some abdominal discomfort or pain. The abdomen becomes swollen and tumid, often mainly tympanitic at first, and in children the condition may resemble that of chronic intestinal catarrh. As the case progresses the distension is gradually seen to be not entirely tympanitic, and evidence of free fluid becomes obvious and more distinct. In some cases the onset of ascites is sudden. As a rule, the amount of

<sup>1</sup> Morgagni, 1867, ix.

<sup>2</sup> Johns Hopkins Hospital Bulletin, 1901, xii, 293.

fluid is not extreme, and if removed reaccumulates slowly; but in adults with existing hepatic cirrhosis the ascitic distension may be indistinguishable from that due to uncomplicated cirrhosis. The distended abdomen is tender on pressure. The pressure of a large ascitic effusion on the inferior vena cava may cause some œdema of the feet and even a trace of albumin in the urine. The ascitic fluid may be clear, turbid, or even blood-stained, and may coagulate when removed. As pointed out elsewhere, the contained cells are mainly lymphocytes. The opsonic index of the effusion is lower than that of the blood serum.

2. (a) The suppurative or ulcerative form of encysted tuberculous peritonitis is the most characteristic. The onset of abdominal symptoms is, as in the ascitic form, preceded by failing health and an irregular temperature. The abdomen becomes swollen and tumid, often first in the lower part, and there is a complaint of abdominal discomfort and tenderness, and of griping pains. The abdominal pain is made worse by walking and by jarring. The abdomen gradually becomes more distended, and the existence of fluid is suspected, but being more or less encysted is often difficult to determine. On palpation the abdomen feels doughy and tumor-like masses due to enlarged glands, adherent coils of intestine, or the rolled up omentum may be felt through the abdominal wall. The thickened omentum forms a characteristic hard cord running transversely across the upper part of the abdomen; there is usually resonance above it, which enables it to be distinguished from the margin of the liver. The tumors are usually fixed, tender on pressure and usually dull on percussion. The amount of distension and the distinctness with which these pseudotumors can be felt vary from time to time. This depends on changes in the amount of exudation and in the quantity of gas in the intestines. In advanced cases the umbilicus may become indurated and inflamed from an abscess pointing there; although this should always suggest the possibility of tuberculous peritonitis, it is not pathognomonic, for a localized pneumococcic abscess may discharge at the umbilicus, and so may an abscess in puerperal infection. Percussion is painful and shows irregular areas of resonance, due to tympanitic distension of intestinal coils, and of dullness due to localized exudation. Rectal or vaginal examination may reveal the presence of tumors due to glands, matted coils of intestine, or salpingitis.

(b) In the ascitic form of encysted peritonitis the collection of serous fluid may simulate an abdominal cyst, especially in women.

3. In the obliterative form the clinical manifestations are often vague. They may be mainly those due to interference with the functional activity of the alimentary canal, dyspepsia, flatulence, constipation, and pain; or there may be palpable tumors. Some cases with universal adhesions may not present any symptoms, but in others the intestinal movements may be so interfered with as to give rise to chronic obstruction. Symptoms of chronic intestinal obstruction may be brought about by peritoneal adhesions at one point; or in rare instances numerous peritoneal adhesions, no one of which produces definite obstruction, may so obstruct the intestines as to give rise to chronic obstruction; in such a case in a child the visible contracting coils of

intestine may be seen through the abdominal wall. We will pass to a more general consideration of the manifestations that may occur in the anatomical forms of tuberculous peritonitis:

The spleen and less often the liver may be enlarged. Very considerable hepatic enlargement may be due to fatty change, or to concomitant backward pressure. In boys with a patent funicular process between the peritoneal cavity and the tunica vaginalis testis tuberculous thickening may spread down the cord, and hydrocele may result.

The abdominal walls may show prominent subcutaneous veins, and the skin may become harsh, dry, and lose its elasticity. But with abdominal distension it may become shiny; in some instances it is pigmented, and sometimes pigmentation is also seen on the face and may be regarded as indicating some degree of suprarenal insufficiency. There is often a drawn expression, and the face shows signs of grave illness. The condition of the tongue varies; it may be red, irritable, and denuded of epithelium, or furred. Nausea, vomiting, and hiccough are rare. The stools may be colorless and fatty, especially in children, but this change occurs in other cachectic conditions. The temperature is raised in acute and suppurative cases, and may touch 104° F. In many cases there is but slight fever, and in the chronic forms there may be none. From abdominal distension and upward displacement of the diaphragm respiration is embarrassed, and the respiratory movements are rapid, shallow, and mainly costal. The pulse becomes rapid in acute cases, but in the chronic forms is not affected.

The urine does not contain the large quantities of indican seen in acute peritonitis. Ehrlich's diazo reaction may be present, but in 55 cases it was absent in 62 per cent. (Hamman<sup>1</sup>). The urine is high-colored. Albuminuria is not generally considered to be frequent, but Hamman found it in 81 out of 133 cases. Micturition may be painful. In females tubercle bacilli may be found in the vaginal discharge.

The blood shows a moderate secondary anemia, but from concentration of the blood due to ascites or purging there may be an apparent polycythemia. Leukocytosis is not part of the blood-picture of the disease, but it occurs in a certain number of the cases (40 per cent., Emerson; 30 per cent., Shattuck; and 23 per cent., Cabot); and is the result of some complication or secondary infection. A high leukocyte count is more often seen in children; thus the average count in 23 children was 16,435 (Rotch<sup>2</sup>).

Jaundice from compression of the ducts by adhesions has been recorded (Dujon<sup>3</sup>), and may also be due to the pressure exerted by tuberculous glands in the portal fissure, but even this is rare. Ulceration of a tuberculous gland into the hepatic artery has been known to produce an aneurism (Birkhardt and Schümann<sup>4</sup>).

**Complications.**—Extensive tuberculous ulceration of the intestine, especially of the colon, may be suspected when there is diarrhœa with

<sup>1</sup> *Johns Hopkins Hosp. Bull.*, Baltimore, 1908, xix, 256.

<sup>2</sup> *Jour. Amer. Med. Assn.*, 1903, xl, 69.

<sup>3</sup> *Procès-verbaux. XIX Congrès de chir.*, 1906, 166.

<sup>4</sup> *Deut. Arch. f. klin. Med.*, Leipsic, 1907, xc, 288.



offensive stools and blood; bacteriological examination will show tubercle bacilli in the feces. Acute or subacute symptoms suggesting appendicitis, cholecystitis, or pelvic peritonitis may be due to an eruption of miliary tubercles over the peritoneum without any ascites (Armand-Delille<sup>1</sup>). Acute peritonitis may supervene as the result of rupture of a suppurating gland or from perforation of a tuberculous intestinal ulcer. Acute obstruction may be due to a band, or possibly to thrombosis in the tributaries of the mesenteric vessels and paralysis of the corresponding segment of intestine (Johnson<sup>2</sup>).

The thoracic complications are pulmonary tuberculosis and pleurisy, which may be bilateral. A tuberculous pleurisy may exist at the same time as an active tuberculous peritonitis, precede it, or come on when the peritoneal lesion has ceased to be clinically manifest. Symptoms suggesting subacute intestinal obstruction—namely, constipation and vomiting—may be in reality due to the onset of tuberculous meningitis.

**Diagnosis.**—The presence of tuberculosis elsewhere is an important factor. In children tuberculous infection of the peritoneum is much the commonest cause of ascites. In women the association of disease of the uterine adnexa should always suggest a tuberculous origin for ascites or chronic peritonitis.

In some rather rare cases there may for a time be a very considerable resemblance to typhoid fever. The most certain means of distinguishing between these two conditions is by a blood-culture or by the agglutination reaction. When tuberculous peritonitis comes on acutely there may be very great difficulty in deciding whether the condition is due to pneumococcic or tuberculous infection.

It may be very difficult to avoid mistakes in the diagnosis between the ascites of tuberculous peritonitis and that of hepatic cirrhosis. In children hepatic cirrhosis is rare, and when it gives rise to ascites tuberculous peritonitis is very likely to be diagnosed. In adults the diagnosis is not so difficult, as help is obtained from a history pointing to alcoholism or from the presence of tuberculosis elsewhere. But alcoholism disposes both to cirrhosis and to tuberculosis, and pulmonary tuberculosis is not uncommon in cirrhosis. Further, tuberculous peritonitis may supervene in the course of hepatic cirrhosis, and when this occurs the true nature of the ascites is not likely to be suspected until the fluid is examined. (For cytological diagnosis see pages 529 and 666.)

In simple chronic peritonitis there is an absence of fever, there is less pain, and examination of the fluid after tapping should enable a diagnosis to be made. Some assistance may be obtained by estimation of the opsonic index before and after abdominal massage, a considerable rise in the index pointing to tuberculosis.

Difficulty sometimes arises in deciding whether abdominal distension with fluid and the presence of tumors—omental and glandular—are due to tuberculosis or to malignant disease. In some cases a diagnosis is only made by opening the abdomen. As a rule, an irregular temperature and a history pointing to tuberculosis favor tuberculous

<sup>1</sup> *Presse méd.*, Paris, 1912, xxi, 397.

<sup>2</sup> *Practitioner*, 1906, lxxvi, 332.

infection, which in children is of course much commoner than is intra-abdominal sarcoma. In adults the presence of multiple tumors is more probably evidence of malignant disease. Cases of chronic intussusception in children have been regarded as tuberculous peritonitis.

**Prognosis.**—This may be considered from several points of view: (a) as to immediate recovery; (b) as to relapses of the peritoneal infection; (c) as to complications and remote mechanical effects of adhesions.

(a) As to immediate recovery. The prognosis is different in the various forms of peritoneal tuberculosis. The disease may become arrested and the symptoms disappear without any manifest cause. The improvement may be permanent or only temporary. The prognosis is best in the discrete miliary form with ascites when uncomplicated, and worse in the form with numerous localized foci of purulent exudation. According to F. Taylor, tuberculous peritonitis is probably fatal in more than half the cases, but the general impression is that the outlook is more hopeful than this and that cure occurs in 50 per cent. In estimating the outlook in an individual case, the condition of the general nutrition, the evidence of tuberculosis elsewhere, as in the lungs, the presence of diarrhœa and of a raised temperature must be taken into account. An increased excretion of chlorides in the urine is said to be a sign of improvement. Wasting diarrhœa and persistent fever are bad signs. The prognosis is bad in the presence of complications such as extensive ulceration of the intestines, well-established pulmonary tuberculosis, generalized tuberculosis, meningitis, and evidence suggesting rupture of a suppurating mesenteric gland into the peritoneal cavity. It is said that the presence of pleurisy does not make the prognosis worse. An abdominal abscess is a grave sign, but recovery may follow discharge of pus from the umbilicus; a fecal fistula is nearly always fatal.

(b) Recurrence occurs in a certain number of cases. This probably depends on the presence of some source of reinfection in the abdominal cavity—namely, in the intestine, lymphatic glands, vermiform appendix or the Fallopian tubes. The importance of removing the local focus whenever possible has been shown by W. Mayo.<sup>1</sup> On the other hand, in 122 cases of tuberculous peritonitis at all ages, Stone<sup>2</sup> did not find a primary focus in the Fallopian tubes or the vermiform appendix in any case. But the Fallopian tubes are often infected from the peritoneum.

(c) Generalized tuberculosis occurs in a considerable proportion of the fatal cases in children; in 26 fatal cases this was noted in 13 (Rolleston<sup>3</sup>). The remote mechanical effects are due to peritoneal adhesions which may give rise to internal strangulation of the intestine and acute obstruction. Undoubtedly a considerable proportion of the cases of strangulation by bands occur in patients who have suffered from tuberculous peritonitis, but the number of cases of tuberculous peritonitis in which acute obstruction is due to a band must be small. Since tubercles and peritoneal adhesions may completely disappear, the persistence of adhesions probably depends on a particularly severe form of peritonitis or, more

<sup>1</sup> *Jour. Amer. Med. Assn.*, 1904, xliv, 1157.

<sup>2</sup> *Boston Med. and Surg. Jour.*, 1908, clviii, 705.

<sup>3</sup> *Brit. Med. Jour.*, 1911, ii, 473.

probably, on the persistence of a tuberculous focus in the peritoneal cavity.

**Treatment** may be divided into (1) medical, (2) by injection of vaccines, (3) hygienic measures, and (4) by surgical means.

**Medical.**—The patient should be kept in bed in a well-lighted and airy room. The bowels should be regulated, any tendency to diarrhœa controlled, and constipation obviated. Offensive stools should be treated by guaiacol, which is less irritating than creosote, or if offensive and loose, by salicylate of bismuth. Cod-liver oil and the syrup of the iodide of iron may be given with advantage, but the dose of cod-liver oil should be small at first and the stools should be examined to see that it is being assimilated. Iodine in solution has also been injected under the skin, and good results have been recorded. Mercurial or iodoform ointment, or guaiacol (3j) in anhydrous lanolin (3j) may be rubbed into the skin of the abdomen, which is then covered by a flannel binder. Good results, however, have been reported simply from bandaging.

**Vaccine.**—Treatment is sometimes very successful. Tubercle vaccine (Koch's new tuberculin; T.R.) in doses of  $\frac{1}{2000}$  mg. of the powdered vaccine is given hypodermically, and is not increased above  $\frac{1}{600}$  mg. Riviere<sup>1</sup> advises  $\frac{1}{12000}$  to  $\frac{1}{8000}$  mg. for a child of one year,  $\frac{1}{4000}$  mg. for a child of five years, and  $\frac{1}{3000}$  mg. for children of ten to twelve years. If human tuberculin fails a trial may be given to bovine tuberculin.

**Hygienic Treatment.**—Very satisfactory results follow moving the patient in the early stages into the country and especially to the seaside, with the adoption of open-air treatment. This should be adopted as early as possible, and continued until recovery has been established.

**Surgical Treatment.**—Laparotomy is contra-indicated in widespread tuberculosis, in infants under a year old and in the presence of pulmonary tuberculosis. It is necessary when an abscess forms or when acute intestinal obstruction occurs; and it is useless in the obliterative and adhesive form. The question of operative interference, therefore, mainly concerns the ascitic form. The operative treatment really dates from 1862, when Sir Spencer Wells opened the abdomen of a woman twenty-two years of age, but instead of an ovarian cystadenoma, as had been anticipated, found widespread peritoneal tuberculosis; the abdomen was emptied, and after a sharp attack of peritonitis the patient got well and remained so. Treatment by laparotomy with simple evacuation of the ascitic fluid was thus started, and in 1890 König published 131 cases, with 84 recoveries. It was supposed that operation reduced the rather feeble vitality of the peritoneal tubercles, and thus led to their death. The way in which the withdrawal of fluid acts is now explained in the following manner: peritoneal tuberculosis, being a local infection, the opsonic index of the ascitic fluid is lower than that of the blood-plasma; hence, if the ascitic fluid be removed, it enables a fresh effusion from the blood to occur; the opsonic index of this recurrent effusion is higher than that of the original one, and therefore exerts a curative effect on the local tuberculous process. If this were the only

<sup>1</sup> *Brit. Med. Jour.*, 1907, ii, 1131; and *Tuberculin Treatment*, 1913, Oxford.



object to be aimed at, simple paracentesis should be equally effective. Cures have indeed followed paracentesis alone, or followed by the injection of an emulsion of iodoform (Schömann<sup>1</sup>) or of oxygen (Schulze<sup>2</sup>) into the peritoneum. The utility of laparotomy is, however, by no means confined to removal of the ascites; it is important to take away, when possible, the primary focus of tuberculous infection, such as the Fallopian tubes or the vermiform appendix, so as to prevent continued infection and a relapse. The question whether laparotomy gives better results than medical treatment has been extensively discussed, and numerous statistics have been brought forward by surgeons and physicians to support their respective lines of treatment. At the present time opinion is still somewhat divided between these two views.

Patients to be submitted to laparotomy should be selected; and as they are therefore those in which the prognosis of a spontaneous cure is favorable, the question has naturally been much debated whether laparotomy really exerts a beneficial influence. It is probable that when employed in suitable cases laparotomy does accelerate a cure. Medical and hygienic treatment should be tried first, and if improvement follows should be persisted in. If improvement does not occur in four or six weeks operation is indicated, unless there be some reason to the contrary. Any sign of increase in the activity of the disease should lead to earlier operation.

### TUMORS OF THE PERITONEUM

The subject of new-growths of the peritoneum will be considered under the following heads:

1. Non-malignant tumors. (a) Solid. (b) Cystic.
2. Malignant growths. (a) Primary. (b) Secondary.

#### Non-malignant Tumors

These are not so rare as primary malignant tumors of the peritoneum, but this is mainly due to the inclusion, among innocent tumors, of cysts which are commoner than the solid innocent growths.

**Solid Non-malignant Tumors.**—**Fibromas, Fibromyomas, and Myomas.**—In the first place circumscribed thickenings of the peritoneum due to attrition, such as the lamellar fibromas on the surface of an enlarged spleen, or those due to chronic inflammation, such as the fibrous plaques sometimes present in chronic peritonitis, fibrosed tubercles, and pseudo-tubercles must be excluded from consideration. A lamellar fibroma has been known to form around a piece of steel (Shattock<sup>3</sup>).

Although not intraperitoneal tumors, attention may be directed to the fibrous desmoid tumors of the anterior abdominal wall, which, although innocent, are sometimes erroneously described as fibrosarcomas. They occur mainly in women, especially in multiparæ and during pregnancy,

<sup>1</sup> *Zentralbl. f. Chir.*, Leipsic, 1904, xxxi, 1409, Orig.

<sup>2</sup> *Mitt. a. d. Grenzgeb. Med. u. Chir.*, Jena, 1907, xviii, 180.

<sup>3</sup> *Transactions of the Pathological Society of London*, 1893, xlv, 151.

and it has been said that the protuberance of the abdomen favors their development. They are more often below than above the umbilicus; they are equally common on the right and left sides. They arise from the sheath of the rectus muscle, from the neighboring aponeuroses, from the iliac crest (Nélaton), from tendons (Doran), or possibly from the round ligament of the uterus. They may be multiple. In 400 cases of connective-tissue tumors of the abdominal wall collected by Pfeiffer,<sup>1</sup> 87 per cent. were in women.

Pure *fibromas* are rare, they are usually single and of considerable size, and are found in connection with the mesentery, omentum, or the retroperitoneal space. They probably arise from proliferation of pre-existing fibrous tissue in these positions, but Belkowsky<sup>2</sup> described a hard fibroma which he believed was derived from an appendix epiploica. Whitney<sup>3</sup> described a special group of fibromas arising from the sub-peritoneal tissues of the true pelvis. The tumors are composed of oedematous fibrous tissue enclosing some endothelial cells, and may produce hernial protrusions in the perineum, ischiorectal region, labium, or scrotum. Of Whitney's 19 cases, 15 were females and 4 males. They may reach a very considerable size.

Some apparently fibrous tumors growing from the retroperitoneal space and from the root of the mesentery contain smooth muscular fibres, which may be derived from Treitz's muscle in the root of the mesentery, and are really fibromyomas. The tumor may pass between the layers of the mesentery and form a solid mesenteric tumor. In 32 cases of fibroma, fibromyomas, or myoma of the mesentery, collected by Greer,<sup>4</sup> 11 were in females, thus disproving the view that these tumors are necessarily of uterine or broad ligament origin. Fibromas and fibromyomas are encapsulated and shell out readily; they may show mucoid degeneration with the formation of spaces in their substance, and so resemble cystic fibromyomas of the uterus. Fibromyomas, or possibly in rare instances myomas, of retroperitoneal origin may be multiple.

The *clinical aspects* depend upon the position of the tumor. The special feature of the fibromas arising in the true pelvis—viz., the tendency to give rise to hernial protrusions—has already been referred to. The symptoms come on slowly, pain is absent in most instances, and intestinal obstruction, which is not uncommonly brought about by mesenteric cysts, does not seem to occur. The correct diagnosis is very difficult, and these tumors are very likely to be regarded as ovarian cysts or uterine fibromyomas.

The *treatment* is surgical, and consists in removal. Of 27 fibromas or fibromyomas of the mesentery removed by operation, 20 recovered (Greer). A *ganglionated neuroma* derived from the sympathetic has been found in the mesentery (McNaughton-Jones<sup>5</sup>) and a *neuromyoma* of the mesentery has been described (Paterson<sup>6</sup>).

<sup>1</sup> *Beitr. z. klin. Chir.*, Tübingen, 1904, xliv, 334.

<sup>2</sup> *Rev. méd. de la Suisse Romande*, Geneva, 1893, 431.

<sup>3</sup> *Annals of Surgery*, 1905, xli, 823.

<sup>4</sup> *Brit. Med. Jour.*, 1911, ii, 1085.

<sup>5</sup> *Proc. Roy. Soc. Med.*, 1912, v, (Obst. and Gyn. Sect.), 287.

<sup>6</sup> *Lancet*, London, 1913, ii, 997.

**Lipomas** may arise in the abdominal cavity (1) in connection with hernial orifices, the inguinal, femoral, or obturator rings, and in weak spots or defects in the linea alba. Overgrowth of fat in these positions may exert traction and so pull out a process of the parietal peritoneum and thus give rise to hernia. They may cause pain and vomiting, which, unless their presence is detected, are difficult to explain (Anderson<sup>1</sup>). (2) In rare instances they arise from giant-growth of an appendix epiploica; Gruber<sup>2</sup> recorded a large pedunculated lipoma which formed the only content of a left scrotal hernia. (3) From the fat around the kidneys and in the iliac fossæ; they lie under the prerenal fascia which separates them from the colon, intestines, and pancreas. These lipomas are rather more common on the right side and may remain retroperitoneal, or may work their way between the layers of the mesentery, mesocolon, omentum, or, in very rare instances, of the broad ligament (Middelshulte,<sup>3</sup> Peyrot,<sup>4</sup> Treves,<sup>5</sup> Borrmann<sup>6</sup>), and so become more or less pedunculated. The transverse colon may become surrounded by the adipose growth. They are usually single, but may show signs of fusion of separate tumors. They may be composed of fat only or of fat mixed with fibrous tissue, show myxomatous degeneration, calcareous infiltration, or very rarely contain cartilage. Very exceptionally sarcomatous change has supervened. They may be encapsuled, or shade off into the retroperitoneal fat from which they arise. Most of the recorded instances have weighed over twenty pounds, and about 6 have been more than fifty pounds. In Buckner's<sup>7</sup> case, a fibrolipoma arising in the subperitoneal tissue of the true pelvis weighed 268 pounds.

*Etiology.*—The large lipomas, which are decidedly rare, are more frequent in women than in men; thus, out of 84 cases 61, or 73 per cent., were in females, and 23, or 27 per cent. in males (Proust and Treves<sup>8</sup>). The usual age is between thirty and fifty years, but isolated examples have been recorded in children (Lauwers). They are not necessarily associated with general obesity. Of Proust and Treves' 89 collected cases, 14 were parietal, 38 perirenal, and 37 mesenteric. Ten were multiple and the remainder single tumors.

*Physical Signs.*—Unless of a large size, they are not likely to be detected, as from their soft consistency they are difficult to feel. They grow slowly, so that the increase in size of the abdomen is gradual. When palpable, the tumor is soft, smooth, free from tenderness, and semifluctuating, so that ascites, either general or encysted, is commonly suspected, although ovarian or hydatid cysts have been diagnosed. As growth proceeds, the abdominal distension, which is mainly in the anteroposterior diameter, increases, the diaphragm is pushed up and the contents of the thorax pressed upon. The later stages are attended

<sup>1</sup> *Brit. Med. Jour.*, 1896, ii, 1087.

<sup>2</sup> *Virchows Archiv*, 1885, cii, 541.

<sup>3</sup> *Inaug. Diss.*, Griefswald, 1884.

<sup>4</sup> *Bull. Soc. anat.*, Paris, 1875, 3s., x, 178.

<sup>5</sup> *Transactions of the Clinical Society of London*, 1893, xxvi, 101.

<sup>6</sup> *Virchows Archiv*, 1907, clxxxix, 436.

<sup>7</sup> Quoted by Whitney, *Annals of Surgery*, 1905, xli, 823.

<sup>8</sup> *Rev. gyn. et de chir. abdom.*, 1908, xii, 93.



with general wasting and œdema of the feet; malignant disease may then appear probable.

*Symptoms.*—The progress of the disease is slow, the general health and nutrition are well maintained, and symptoms do not appear for a long time. They include a feeling of weight, fulness, and discomfort from abdominal distension, sometimes gastro-intestinal symptoms from pressure on the stomach and intestines, inconvenience from pressure on the urinary bladder, and sooner or later dyspnoea from the upward displacement of the diaphragm.

*Diagnosis* from ascites is extremely difficult, as such a rare condition as a lipoma is only likely to be suspected after the abdomen has been unsuccessfully tapped. From malignant disease their slow course is the main distinction. From ovarian and hydatid cysts they differ in their softness and indefinite outlines. Difficulty has occurred in distinguishing them from large lipomas of the abdominal wall.

*Prognosis.*—This depends upon their being operated upon before they have reached a very large size, for if left alone the patients gradually emaciate and die. In 26 cases in which the tumor was wholly or partially removed, recovery followed in 12, with recurrence in one (Adami<sup>1</sup>).

*Treatment.*—The only radical method is surgical, but the results of removal differ in those that are entirely retroperitoneal and in those that are pedunculated or situated in the omentum. Removal of a retroperitoneal lipoma has, in some cases, deprived a considerable extent of the intestine of its blood-supply, and so led to gangrene or necessitated resection of part of the intestine. In 31 retroperitoneal lipomas operated on the mortality was 51.6 per cent. (Reynolds and Wadsworth<sup>2</sup>).

**Angioma** is very rare, but the line dividing them from angiosarcoma is rather thin. In Julliard's<sup>3</sup> case a cavernous angioma of the mesentery was as large as an adult's head, and produced intestinal obstruction. A cavernous angioma of the transverse mesocolon was diagnosed as a twisted mesenteric cyst (Wagener<sup>4</sup>). Lane<sup>5</sup> successfully removed a large degenerating cavernous angioma from the peritoneum of a child aged seven years.

**Myxoma.**—Myxomatous degeneration, of course, occurs in fibromas, myomas, and lipomas, and in some instances the condition may be so advanced as to appear to be a pure myxoma.

**Cysts.**—*Parasitic.* Hydatids, cysticercus.

*Non-parasitic.*—Mesenteric, omental, sanguineous, retroperitoneal hematoma, dermoid, retroperitoneal, urachal, conditions simulating cysts.

**Hydatid Disease of the Peritoneum.**—Infection of the peritoneum with the cystic or bladder stage of the *Tania echinococcus*, although very striking, is not common; thus, in 1897 cases of hydatid disease, tabulated

<sup>1</sup> *Montreal Med. Jour.*, 1897, xxv, 620.

<sup>2</sup> *Annals of Surgery*, 1906, xli, 61.

<sup>3</sup> *Rev. de gyn. et de chir. abdom.*, 1904, viii, 229.

<sup>4</sup> *Zentralbl. f. Gynäk.*, Leipsic, 1904, xxviii, 1600.

<sup>5</sup> *Transactions of the Clinical Society of London*, 1893, xxvi, 5.

by Davies Thomas,<sup>1</sup> the peritoneum, omentum, and mesentery were affected primarily in 26, or 1.4 per cent., only. From a review of 2727 cases Dévé<sup>2</sup> concludes that peritoneal hydatidosis is always secondary. No statistics exist to show that hydatid disease of the peritoneum was commoner in the early part of the last century when Bright gave such a graphic account of its clinical features, but the practice then in vogue of tapping these cysts through the abdominal walls with a trocar offered great facilities for infection of the peritoneal cavity.

The method by which infection of the peritoneum with hydatid cysts takes place is probably not always the same. In cases with a large number of cysts implanted on the peritoneum the most probable explanation is that rupture or leakage from a single and primary cyst, usually in the liver, has infected the peritoneum. It appears to take about two years for cysts thus implanted on the peritoneum to become sufficiently large to give rise to signs and symptoms. Admixture of bile with ascitic fluid does not prevent secondary infection of the peritoneum with hydatid cysts (Dévé<sup>3</sup>). On the other hand, in instances in which a single cyst or only a few cysts occur in the retroperitoneal tissue, a very common position being between the prostate and the rectovesical fascia, the embryo may have burrowed from the bowel or from the bloodvessels in the neighborhood toward the peritoneum. Cranwell,<sup>4</sup> who has collected 56 examples of retrovesical hydatid cysts in males, believes that most of the retrovesical cysts are due to peritoneal infection.

*Morbid Anatomy.*—The number of cysts may be enormous when the infection is secondary to rupture of a preëxisting cyst; the omentum, mesentery, and visceral peritoneum may be almost universally affected, but the omentum and pelvis are the most frequent sites. The cysts may be of almost any size, from a pinhead upward; when single or few, the cysts tend to be bigger than when large numbers are present. The cysts may project from the surface of the viscera, be sessile on the peritoneum, especially on the omentum, mesentery, and pelvis, be pedunculated, and in rare instances a cyst may lie free in the abdominal cavity. Pedunculated hydatids may be sterile, probably from a deficient nourishment. The cysts may be separate or crowded together. According to Stirling and Verco,<sup>5</sup> adhesions around uninfamed cysts occur only after injury or operative interference. Chronic peritonitis may be set up by mechanical irritation, and may lead to the formation of a thick fibrous capsule over dependent or other cysts, such as those in Douglas' pouch, exposed to friction; calcification may subsequently occur. A rare condition of "pseudotuberculosis" of the peritoneum may follow rupture of a cyst, and consists of (1) minute developing cysts and (2) of small nodular granulomas containing hooklets or pieces of hydatid membrane scattered over the surface of the peritoneum.

Suppuration may take place in one or more of the cysts and set up

<sup>1</sup> *Hydatid Disease*, Adelaide, 1884.

<sup>2</sup> *Compt. rend. Soc. biol.*, Paris, 1913, lxxiv, 735.

<sup>3</sup> *Compt. rend. Soc. biol.*, Paris, 1903, lv, 75.

<sup>4</sup> *Rev. de gyn. et de chir. abdom.*, Paris, 1907, xi, 606.

<sup>5</sup> *System of Medicine* (Allbutt and Rolleston), 1907, vol. ii, Part 2, p. 999.

a localized abscess, general peritonitis, or pylephlebitis and multiple abscesses in the liver (Ogle<sup>1</sup>).

*Clinical Aspect.*—The enlargement of the abdomen is gradual, and may continue for years; in one of Bright's<sup>2</sup> cases it had lasted for at least ten years. There may be either a diffuse swelling, or separate cysts can be made out, not only by palpation, but with the eye. The cystic tumors are often so firm as to suggest solid growths, they are freely movable, alter their position with that of the body, and are not obviously connected with any of the abdominal viscera. A hydatid thrill is rare, and as it may be present over other cysts, such as ovarian or mesenteric, and even in ascites, too much stress must not be laid on it. When the abdomen becomes very greatly distended the diaphragm is pressed up and respiration is much embarrassed, while pressure on the stomach and intestines may lead to dyspepsia, constipation, or, in very rare instances, to intestinal obstruction (Hutchinson<sup>3</sup>). As the result of pressure on the inferior vena cava, the superficial abdominal veins may become very prominent and the urine scanty and high-colored. A retro-vesical cyst in the pelvis may press on the rectum, bladder, and ureters, and may thus imitate a hypertrophied prostate, or lead to hydronephrosis, consecutive kidney disease, and pyelonephritis. Out of 24 autopsies on such cases, the ureters were dilated in 11 (Cranwell). There is vesical pain, frequent micturition, constipation, and a feeling of weight in the perineum.

*Diagnosis.*—If multiple cystic tumors can be felt, the true solution is not difficult, but when the patient is a woman and one or two cysts only are palpable, the disease may be thought to be ovarian cystadenomas or even uterine fibromyomas. The history that a hydatid cyst of the liver has existed or has been tapped would be strongly in favor of hydatid infection of the peritoneum. From multiple abdominal malignant disease the slow course and evidence that the tumors are cystic should distinguish it. Exploratory puncture is dangerous, as anaphylactic symptoms and even death may follow escape of hydatid fluid into the peritoneal cavity. If it be done, the discovery of scolices, hooklets, or of the characteristic laminated ectocyst, will make it certain that a hydatid had been aspirated; chemical analysis, however, does not settle the question, for some hydronephroses contain fluid of a very similar composition (Stirling and Verco). Eosinophilia, a specific precipitin reaction, and fixation of the complement when positive points to hydatid infection, but a negative result is inconclusive.

*Treatment.*—A single cyst should be fully exposed and dealt with surgically; when the cysts are manifestly multiple, operation is still the only available means of treatment, but the result is not likely to be so satisfactory as with a single cyst. Dévé<sup>4</sup> urges that large sessile cysts should be injected with formol (2 per cent.) and the contents removed, and that small sessile cysts should be injected with formol only. In no

<sup>1</sup> *St. George's Hospital Reports*, 1867, ii, 347.

<sup>2</sup> *Clinical Memoirs on Abdominal Tumors*. New Sydenham Society.

<sup>3</sup> *Med.-Chir. Trans.*, London, 1894, lxxvii, 133.

<sup>4</sup> *Normandie Méd.*, Rouen, 1912.



case should a cyst be tapped through the abdominal wall. A single cyst in the pelvis may be opened through the perineum or vagina, but Cranwell recommends Tuffier's median incision above the pubes. The outlook in these retrovesical cysts is grave, as of 56 cases 25 proved fatal (Cranwell).

*Cysticercus cellulosæ* is, in rare instances, met with in great numbers inside the abdomen, chiefly in the mesentery, but this condition gives rise either to insignificant or to no clinical symptoms.

**Mesenteric Cysts.**—This term has sometimes been applied to cysts in the omentum and mesocolon, but it is better to limit it to cysts in the mesentery of the small intestine and to employ it solely as descriptive of the position of the cyst.

*Pathogeny.*—Proust and Monod<sup>1</sup> describe the following forms of mesenteric cyst: (1) Derived from the remains of embryonic epithelium (*a*) of intestinal origin; Terrier and Lecène<sup>2</sup> collected 18 "enteroid" or juxta-intestinal cysts which they regard as derived from the remains of Meckel's diverticulum. Multiple cysts near the commencement of the jejunum may be the result of sequestrations from the intestine; Carnot<sup>3</sup> showed experimentally that pieces of mucosa of the stomach and gall-bladder when implanted on the intestine formed cysts, and Walker-Hall<sup>4</sup> described a mesenteric cyst lined by gastric mucosa with parietal cells. (*b*) From the remains of the Wolffian body. (*c*) Dermoid cysts are infrequent; they may lie between the layers of the mesentery or be attached to its surface and be pedunculated. (2) Serous cysts, lined by endothelium and due to distension of closed peritoneal pouches; they are very rare in the mesentery of the small intestine. (3) Lymphatic cysts may be simple or chylous. The latter contain lymphoid tissue in their walls, and constitute the most important group of mesenteric cysts. Brinsmeade<sup>5</sup> found the sex incidence equal in 44 chylous cysts, and states that they may be congenital or occur late in life.

*Morbid Anatomy.*—Usually unilocular these cysts are occasionally multilocular. The cysts may project from the free border of the intestine or from its mesenteric border and may then pass between the layers of the mesentery. Cysts may be embedded in the layers of the mesentery without any direct connection with the intestine. Their surface is covered by peritoneum and their walls are composed of fibrous tissue; they may contain smooth muscular fibres very irregularly arranged, and some fat. There may be no layer of epithelium on the interior of the cysts, which may be lined by granulation tissue.

The contents may be clear and serous, containing albumin and cholesterol; turbid, viscid, with mucin; chylous, with the chemical composition of chyle. Timball<sup>6</sup> collected 49 cases of mesenteric cysts with hemorrhagic contents. Turnure<sup>7</sup> has collected 50 cases of gaseous cysts in

<sup>1</sup> *Rev. de gyn. et de chir. abdom.*, Paris, 1912, xix, 225.

<sup>2</sup> *Rev. de chir.*, Paris, 1904, xxix, 161.

<sup>3</sup> *Arch. de méd. expér. et d'anat. path.*, Paris, 1905, xvii, 273.

<sup>4</sup> *Jour. Path. and Bacteriol.*, Cambridge, 1908, xii, 128.

<sup>5</sup> *Annals of Surgery*, 1908, xlviii, 565.

<sup>6</sup> *Rev. de chir.*, Paris, 1910, xli, 45.

<sup>7</sup> *Ann. Surg.*, Phila., 1913, lvii, 811.

connection with the intestine; they have been regarded (1) as true neoplasms which secrete gas from the blood, and in this respect comparable with the air bladders of fishes (Mair<sup>1</sup>), (2) as due to bacteria, or (3) as purely mechanical. Skiagraphy shows marked luminosity of the abdomen.

*Physical Signs.*—The cyst is round, well-defined, tense, elastic, movable, is usually on the right side of the abdomen a little below the umbilicus, and is not connected with any of the viscera except the intestines. It is dull on percussion, is surrounded by resonant intestine, and there may be a band of resonance due to the attached piece of intestine running across it.

*Symptoms.*—A sudden attack of abdominal pain is usually the first indication of the existence of a mesenteric cyst; there may be recurrent attacks of colic and vomiting; while in a number of the instances acute intestinal obstruction has resulted from kinking of the intestine. On the other hand the symptoms may be those of gastro-enteritis.

*Diagnosis* is often difficult, and when the cyst is detected, must be made from a distended gall-bladder, hydatid cysts hanging down from the liver or in the peritoneum, floating kidney, ovarian or parovarian cysts of small size with a long pedicle, solid tumors of the mesentery or omentum, pancreatic cysts which are much larger, and even an appendicular abscess. No exploratory tapping is permissible.

*Treatment* is surgical, and consists in the enucleation of the cyst when this is possible, if not in drainage. These cysts should be operated upon without waiting for urgent symptoms.

**Omental Cysts.**—The omentum may be the seat of cysts of various kinds, such as hydatid and “dermoid,” which are referred to elsewhere. Hasbrouck<sup>2</sup> distinguished (1) true cysts inside the omentum of which he has collected 20 examples from (2) cysts attached to the omentum, of which he collected 12. Multiple cysts possibly due to lymphatic obstruction have been recorded. Gairdner,<sup>3</sup> Braithwaite,<sup>4</sup> Mathews<sup>5</sup> and others have described large single cysts with clear contents, possibly cystic lymphangiomas. Hemorrhage may take place into these omental cysts (Jacobi<sup>6</sup>). They have naturally been regarded as due to congenital aberrations; possibly some are, like the retroperitoneal cysts, derived from the Wolffian body, but Firket<sup>7</sup> believes that proliferation of the peritoneal epithelium may form multiple small cysts. Of 22 cases quoted by Fort,<sup>8</sup> 50 per cent. were under ten years of age, and three-fourths were females.

The condition does not appear ever to have been definitely diagnosed before the abdomen was opened. Symptoms are not prominent in the early stages of growth, and pain usually leads to examination of the abdomen and the detection of a cyst which is superficial in position and usually movable to a limited extent.

<sup>1</sup> *Journal of Pathology and Bacteriology*, Cambridge, 1908, xii, 433.

<sup>2</sup> *Annals of Surgery*, Philadelphia, 1908, xlviii, 206.

<sup>3</sup> *Transactions of the Pathological Society of London*, 1852, iii, 374.

<sup>4</sup> *Lancet*, London, 1898, ii, 1472.

<sup>5</sup> *Brit. Med. Jour.*, 1905, ii, 1642.

<sup>6</sup> *Transactions of the Association of American Physicians*, 1901, xvi, 232.

<sup>7</sup> *Arch. de méd. expér. et d'anat. path.*, Paris, 1912, xxiv, 697.

<sup>8</sup> *Annals of Surgery*, 1907, xlv, 382.

*Diagnosis.*—Lipomas are the only solid tumors likely to be confused with omental cysts. The large omental cysts may imitate localized tuberculous peritonitis, or ovarian cysts with a long pedicle.

**Peritoneal Sanguineous Cysts.**—Intra-abdominal cysts containing blood may be of various kinds. Thus, hemorrhage may take place into preëxisting cysts, for example, as the result of twisting of the pedicle of an ovarian cystadenoma, or into a mesenteric cyst. Hemorrhage may occur into a soft sarcoma, and malignant hypernephromas may contain more blood than growth. Collections of blood in the female pelvis, which are generally ectopic gestations, ruptured aneurisms, and angiomas, need only be mentioned in order to be distinguished from a fairly definite group of cases, the peritoneal sanguineous cysts (Fisher<sup>1</sup>). Many so-called pancreatic cysts with blood-stained contents are the same as the sanguineous cysts found elsewhere in the peritoneal cavity, and are hemorrhagic effusions into the lesser sac of the peritoneum and therefore peripancreatic, not pancreatic.

*Morbid Anatomy.*—These cysts may also be found in the great and gastrohepatic omentum, mesentery, mesocolon, or project from the peritoneum lining the back of the abdomen. The writer examined a sanguineous cyst arising in the pelvis in a man. The walls of the cysts are composed of well-formed fibrous tissue and may contain some patches of blood pigment. They are usually lined by adherent shaggy fibrin. The fluid is reddish brown and contains blood corpuscles and in some instances cholesterin. In cysts in contact with the pancreas the fluid contains pancreatic ferments. Blood-clot in various stages of change may be found in these cysts. Large nucleated cells—probably endothelial and derived from the peritoneum—also occur in the fluid.

*Pathology.*—These cysts are probably the result of traumatic hematomas, but as the cyst may not become manifest until some time has elapsed since the injury, it has been suggested that local peritonitis first occurs and later hemorrhage from the newly formed vessels.

*Clinical Features.*—The cyst is much commoner in the upper than in the lower half of the abdomen, and is usually in the middle line. It forms a large, tense tumor, may have pulsation conducted to it from the aorta and can be shown by percussion to be distinct from the liver. Symptoms are less marked than in pancreatic cysts, and after reaching a considerable size the tumor may remain unaltered for years.

*Diagnosis* of peritoneal sanguineous cysts other than those around the pancreas is very difficult. This is mainly due to their rarity.

*Treatment* is surgical and consists in draining the cyst. Excision is rarely possible, as the walls are so often part of the peritoneum forming the mesentery, lesser omentum, or mesocolon. Cure has followed tapping, but it is dangerous and should not be attempted until the cyst is exposed by laparotomy.

**Retroperitoneal hematomas** are rare; they may be due to trauma, such as rupture of the kidney, bursting of an abdominal aneurism, or leakage from a hemorrhagic retroperitoneal or renal sarcoma. In some instances

<sup>1</sup> *Guy's Hospital Reports*, 1893, xlix, 275.



the source of the blood is not clear. The blood tracks down behind the peritoneum toward the pelvis, and may form a distinct tumor accompanied by pain. On the right side such a tumor may suggest appendicitis. The symptoms may be those of acute intestinal obstruction.

**Dermoid cysts** in rare instances occur in the peritoneum without any evidence that they were directly derived from the ovaries. Thus, Pakowski<sup>1</sup> collected 74 of these dermoid cysts, 31 of which were connected with the mesentery of the small intestine. These cysts may be simple or composed of skin only, or composite or embryomas. They are usually found in females, but Pakowski collected 6 dermoids of the mesentery in males. They may occur between the layers of the mesentery, omentum, and transverse mesocolon, or in the retroperitoneal space. In some instances, however, a "dermoid" cyst originating in the ovary may become detached and subsequently contract adhesions elsewhere. Multiple "dermoid" cysts may be due to rupture of an ovarian embryoma with the resulting implantation of fragments over the peritoneum; the multiple growths are not malignant, but resemble the implantations sometimes associated with ovarian papillomas. Suppuration occasionally occurs in these cysts, and in rare instances, of which Montgomery<sup>2</sup> has collected 10 cases, the teratomas become malignant.

**Retroperitoneal Cysts.**—Cysts manifestly arising in viscera behind the peritoneum, the kidneys, adrenals, and pancreas, are not included in this category. Although far from common, cysts of various kinds may be found in the subperitoneal connective tissue; for example, hydatids. A multilocular cyst, structurally resembling an ovarian cystadenoma, may occur in the retroperitoneal tissues of men as well as of women. These cysts may arise close to the kidney and be mistaken for a floating kidney, a hydronephrosis, or on the left side for a primary neoplasm of the tail of the pancreas. Severe attacks of pain, simulating Dietl's crises or those of appendicitis (Elder<sup>3</sup>), may occur. The cysts may pass between the layers of the mesentery, omentum, mesocolon, or mesorectum, and in all probability are derived from sequestrations of the Wolffian body. They may contain several pints of fluid. The multilocular cysts may become malignant and give rise to metastases.

Among rare conditions cystic dilatation of the receptaculum chyli and collection of fluid in a subcecal pouch, the mouth of which has been closed, may be mentioned.

**Urachal Cysts.**—The urachus may be partially pervious; thus minute cystic dilatations were found in 24 out of 74 cases specially examined by Wutz.<sup>4</sup> In rare cases there are cysts containing many pints of fluid. In some instances the cysts communicate with the bladder; infection may then spread into the cyst; in other instances the cyst and the urinary bladder are connected by an impervious cord. The contents may be clear, turbid, blood-stained, or purulent. The cysts are usually in front of the peritoneum and adherent to the umbilicus and anterior abdominal

<sup>1</sup> *Arch. gén. de chir.*, Paris, 1912, vi, 1029.

<sup>2</sup> *Jour. Exper. Med.*, 1898, iii, 259.

<sup>3</sup> *Montreal Medical Journal*, 1905, xxxiv, 891.

<sup>4</sup> *Virchows Archiv*, 1883, xcii, 387.

wall, but may be intraperitoneal; the latter position is explained by a persistence of the fetal mesentery of the urachus (Delore and Cotte<sup>1</sup>). The wall contains smooth muscular, elastic and fibrous tissue, and may show epithelium resembling that of the bladder, but this may be detached. The cysts are usually unilocular, but in Doran's<sup>2</sup> case there were two cysts. Weiser<sup>3</sup> tabulated 89 cases, but included 19 "allantoic" cysts (see *infra*), so that the number of authentic cases on record is not so great. They occur chiefly in women, but have been met with in men and in children. A case in a man, in St. George's Hospital, was diagnosed correctly before operation. In Weiser's 89 cases females were about three times more often affected than males. The cysts are in the middle line between the umbilicus and the pubes; they may be soft and fluctuating, resembling a distended urinary bladder, or firm and apparently solid. There may be pain in the lower part of the abdomen, probably from associated local peritonitis. They may imitate encysted peritonitis, especially of tuberculous origin, and ovarian cystadenomas.

The *treatment* of urachal cysts is surgical. In some instances they can be dissected out, in others the only available course is drainage. It is important that the relation of the cyst to the bladder and the possibility of a communication between the two should be borne in mind, otherwise a urinary fistula may follow operation. Tapping the cysts is only a palliative measure, as the fluid is prone to accumulate again.

**Conditions Simulating Peritoneal Cysts.**—Encysted peritonitis may simulate a true cyst. Kelly and Hurdon<sup>4</sup> figure cysts of this nature adherent to the tip of the vermiform appendix. The "allantoic" cysts described by Lawson Tait<sup>5</sup> and B. Robinson<sup>6</sup> in adult women are probably examples of localized pelvic tuberculous peritonitis (Doran).

*Pseudomyxoma* of the peritoneum consists in the presence of numerous encysted collections of gelatinous material in the peritoneum which follows rupture of an ovarian cystadenoma. In about 12 cases, chiefly in males, pseudomyxoma of the peritoneum has been due to the escape of the contents of a mucocele of the vermiform appendix. It may be confused with colloid cancer and with primary tumors derived from the Wolffian body which structurally resemble ovarian cystadenomas.

### Malignant Tumors

*Malignant growths* are more often met with in the peritoneal cavity than innocent tumors, but this depends on the frequency of secondary infection of the peritoneum, for while primary malignant disease and innocent neoplasms of the peritoneum are both rare, primary malignant disease is the more exceptional of the two.

**Primary Malignant Diseases.**—These may conceivably arise in several structures, such as (1) the endothelium of the serous membrane, of the

<sup>1</sup> *Rev. de chir.*, Paris, 1906, 405.

<sup>2</sup> *Medico-Chirurgical Transactions*, London, 1898, lxxxi, 301.

<sup>3</sup> *Annals of Surgery*, 1906, xlv, 529.

<sup>4</sup> *The Vermiform Appendix and its Diseases*, 1905, 311.

<sup>5</sup> *British Journal of Gynecology*, 1887, ii, 328.

<sup>6</sup> *Annals of Surgery*, 1891, xiv, 350.

lymphatics and bloodvessels; (2) the subserous connective tissues, especially around the spine and back of the abdomen, the periosteum of the spinal column and pelvis; and (3) the remains of the Wolffian bodies, Müllerian ducts, accessory adrenal bodies, or even from teratomas that have undergone malignant transformation.

The tumor growth may occupy the omentum or, more rarely, the mesentery or the gastrohepatic omentum, and be thus to all intents and purposes intraperitoneal. In other cases the growth extends behind the peritoneum and to a slight extent displaces the abdominal contents forward; these are cases of retroperitoneal sarcoma. In some instances a growth at first definitely retroperitoneal passes forward, becomes pedunculated, and therefore partly intraperitoneal. Thus, although it might appear to be more logical to describe separately malignant disease (*a*) arising from the peritoneum itself, and (*b*) originating in the tissues (as apart from the organs) of the retroperitoneal space, any such distinction would in reality be artificial.

**Morbid Anatomy.**—Primary malignant tumors of the peritoneum and retroperitoneal space belong to the group sarcoma or endothelioma. Formerly primary carcinoma of the peritoneum was commonly described; alveolar growths resembling carcinoma histologically undoubtedly occur, but are now regarded as endotheliomas and arising in endothelium, either of a lymphatic or bloodvessel or possibly of the surface of the serous membrane (Miller and Wynn<sup>1</sup>). The histological appearances of primary malignant growths of the peritoneum vary considerably; spindle-celled, round-celled, and irregular-celled, alveolar, fibrifying myxosarcoma and lymphosarcoma, endothelioma, and perithelioma (angiosarcoma) all occur. But of 16 primary sarcomas of the omentum 11 were spindle-celled (Bonamy<sup>2</sup>). In some endotheliomas the microscopic appearances are confusing, in some parts resembling carcinoma, in others sarcoma.

The shape of the tumors varies according to their position. Retroperitoneal sarcoma and neoplasms originating between the layers of the great omentum are often flattened out so as to resemble a pancake. Retroperitoneal sarcomas may project forward into the peritoneal cavity and even become pedunculated. There may be multiple pedunculated growths without any manifest primary growth. A primary malignant growth of the peritoneum may be rounded or lobulated. The tumors may reach a considerable size. A primary malignant growth of the great omentum recorded by J. W. Ogle<sup>3</sup> weighed thirty pounds. The origin of primary malignant neoplasms is more rarely intraperitoneal than retroperitoneal. This depends on the presence behind the peritoneum of structures, such as lymphatic glands, connective tissue, and the remains of the Wolffian body and Müllerian duct, from which tumors may arise. As a rule, primary peritoneal and retroperitoneal tumors do not invade adjacent organs to any great degree. It may, however, be difficult to determine the exact origin of a malignant growth, and in

<sup>1</sup> *Journal of Pathology and Bacteriology*, Cambridge, 1908, xii, 267.

<sup>2</sup> *Rev. de gynéc.*, Paris, 1908, xii, 285.

<sup>3</sup> *St. George's Hospital Reports*, 1867, ii, 350.



some instances it must be left an open question whether the growth arose in an organ and spread out of it or whether it started independently of a given viscus in question and subsequently infiltrated it. In such cases the histological appearance of the tumor is the best guide to its origin.

The lymphatic glands and the connective tissues around the aorta and the periosteum of the vertebræ appear to be the commonest starting-points of retroperitoneal sarcoma. A malignant cystic tumor resembling an ovarian cystadenoma, and probably derived from the remains of the Wolffian body, may occur.

Retroperitoneal sarcoma most often arises in the lumbar region and more frequently on the right side, but it may start in the middle line, in the iliac region, or in rare instances in the pelvis. There is frequently some local peritonitis with adhesions over the growth. The tumor is usually firm at first, but in a third of the cases it undergoes central necrosis and becomes cystic (Dutton Steele<sup>1</sup>). The contents may be hemorrhagic, myxomatous or purulent from infection. The pseudocyst has in rare instances opened into the intestine or peritoneum. Thus in a case under my care, a cystic, spindle-celled sarcoma arising near the right kidney opened into the duodenum. The growth may press on the inferior vena cava, the spinal nerves, or on the abdominal viscera. The fixed parts of the colon are more liable to be narrowed by retroperitoneal growths. Tumors in the omentum, which may become cystic, may constrict the colon, and in primary sarcoma of the gastrohepatic omentum, of which Cobb<sup>2</sup> has been able to collect three examples only, the stomach may be depressed downward (A. P. Gould<sup>3</sup>). Secondary growths occur in 33 per cent. of the cases, and are found in the liver, lungs, and peritoneum, and may give rise to ascites.

**Etiology.**—Sex apparently has no influence. In retroperitoneal sarcoma, according to Dutton Steele, the first, fourth, fifth, and sixth decades are most often affected, and 53 per cent. occur between thirty and sixty years of age. Injury has been thought to be a causal factor.

**Clinical Picture.**—The clinical manifestations vary considerably; most commonly there is a deep-seated abdominal tumor with somewhat variable gastro-intestinal symptoms, abdominal distension, and increasing weakness. Although usually fixed, the tumor is occasionally freely movable, especially in the early stages. It may be regular and smooth, or nodular, more or less firm, or may show various degrees of consistency; it may receive transmitted pulsation from the aorta; it is usually not tender on palpation, and is more often to the right of the middle line; a growth in the omentum may resemble a spleen dislocated by extensive deformity of the spine. Primary growths, especially in the omentum, may induce ascites and so imitate tuberculous peritonitis, while a flat retroperitoneal sarcoma, although not palpable, may by pressure on the spinal nerves give rise to severe pain in the back imitating that of aneurism, caries, or malignant disease of the spine, and by compressing

<sup>1</sup> *Amer. Jour. Med. Sci.*, 1900, xcix, 311, and 1904, cxxvii, 939.

<sup>2</sup> *Annals of Surgery*, 1906, xlv, 16.

<sup>3</sup> *Medico-Chirurgical Transactions*, London, 1900, lxxxiii, 257.

the inferior vena cava lead to œdema of the legs, genitals, and lower part of the abdomen with very noticeable enlargement of the subcutaneous abdominal veins. There may be profound anemia before any tumor is palpable. On the other hand, malignant disease of the omentum may produce a large superficial mass forming a kind of shield in front of the intestines or may simulate enlargement of the liver.

The progressive growth of the tumor usually causes pain and sometimes vomiting, constipation, and even intestinal obstruction. The sudden onset of abdominal pain, probably due to extension of the growth setting up local peritonitis, may be the first symptom. The growth may then be sufficiently large to be easily detected. Although the tumor may be of considerable size, the general state of nutrition is less affected than in malignant growths of the stomach or liver of the same dimensions. When retroperitoneal it may be resonant from the presence of intestines, colon, or stomach in front of it. When ascites is present the fluid may be but is not necessarily blood-stained. The fluid may be remarkably viscid from the presence of a "mucoid" body. The course of the disease is somewhat rapid, the average duration of retroperitoneal sarcoma from the onset of symptoms being eight and a half months (Dutton Steele). Death is usually due to exhaustion, but in a few instances has been sudden and due to rupture of the growth and hemorrhage into the peritoneal cavity.

**Diagnosis.**—From the variable character of the symptoms this is very difficult and is usually arrived at only by a process of exclusion. Even although a peritoneal tumor be diagnosed, it is, except when there is definite evidence of other growths, impossible to be absolutely certain that it is malignant unless the abdomen has been opened. Even then removal of a piece of the growth for histological examination is necessary to be absolutely certain, for a considerable number of cases have been recorded in which the abdomen has been opened and closed on the discovery of an inoperable and apparently malignant tumor, and yet the tumor has subsequently disappeared (Greig Smith<sup>1</sup>). These "vanishing tumors" (Power<sup>2</sup>) may possibly, in spite of the absence of any naked-eye evidence, be inflammatory in nature; in some instances a foreign body which has perforated the intestine may be the cause (Bland-Sutton<sup>3</sup>), and it is conceivable that in some the condition was due to actinomycosis or pancreatitis (Bradford<sup>4</sup>). Malignant growths progress more rapidly, produce more marked constitutional symptoms, and give rise to pressure symptoms, such as pain and dilated abdominal veins, in a far greater degree than innocent tumors even though of great size. The differential diagnosis must be made from various conditions, such as pancreatic cysts, renal and suprarenal tumors, malignant disease of the liver (Sailer<sup>5</sup>), aneurism of the abdominal aorta which does not pulsate, retroperitoneal teratomas and innocent tumors, some cases of carcinoma of the colon with suppuration, uterine fibromyomas, and when there

<sup>1</sup> *Medico-Chirurgical Transactions*, London, 1894, lxxvii, 139.

<sup>2</sup> *Lancet*, London, 1899, i, 583. <sup>3</sup> *Ibid.*, 1903, ii, 1148.

<sup>4</sup> *Clinical Journal*, London, 1907, xxi, 76.

<sup>5</sup> *Trans. Coll. Phys.*, Phila., 1912, xxxiv, 328.

is ascites from secondary malignant disease of the peritoneum and from tuberculous peritonitis. A horseshoe kidney, which is met with once in 1600 autopsies, has been mistaken for malignant disease. A nodular mass may resemble fecal accumulation, and enemas and purgatives may then be necessary to settle the diagnosis.

**Prognosis** is extremely grave. Operative interference is impracticable in many cases, especially in extensive retroperitoneal sarcomas. Tumors in the omentum or mesentery are more amenable to removal. Removal of the tumor in an early stage, when it is more or less encapsulated, should lead to better results. In Williams<sup>1</sup> collection of 84 cases of retroperitoneal sarcoma, radical operations were performed in 12 cases, with recovery in 10.

**Treatment.**—Except when removal is possible, treatment is palliative and symptomatic.

**Secondary Malignant Disease of the Peritoneum.**—Synonym: Malignant peritonitis. Secondary infection with carcinoma or sarcoma is far commoner than primary malignant disease of the peritoneum. That it occurs more frequently in women than in men is in part accounted for by influence exerted by malignant disease of the female sexual organs, of the mammae and of the gall-bladder. It chiefly occurs in or after middle life.

**Pathology.**—The primary growth is usually in the abdominal organs. Malignant infection may also extend from the chest, either through the lymphatics of the deep fascia of the parietes from the mamma, described by Handley<sup>2</sup> as “epigastric invasion” of the peritoneum, or less commonly from the cavity of the thorax as in primary carcinoma of the œsophagus. In primary malignant disease of the testes the lumbar glands may convey infection to the peritoneum. In some instances, as in generalized sarcoma, infection reaches the peritoneum by the blood-stream. Primary malignant disease inside the abdomen may spread to some extent by the lymphatics and bloodvessels, or to a limited degree by direct contact. But the chief means of dissemination is the liberation of infective cells, which become widely scattered over the abdominal cavity.

**Morbid Anatomy.**—The tumors may be so minute and discrete as to imitate tuberculous peritonitis, and the condition may then be spoken of as miliary carcinomatosis; in other instances the secondary nodules, being larger and white in color, resemble caseous tubercles, while in some cases, especially of colloid carcinoma, the masses are very large indeed. In women the ovaries may become markedly infiltrated with secondary growth, and as they may form tumors much larger than the primary growth, this sometimes suggests that the original tumor growth started in both ovaries (Bland-Sutton<sup>3</sup>). The miliary growths are less translucent than miliary tubercles, when larger they are, as a rule, white, although they may be hemorrhagic, but they do not caseate and soften. The growths, which are generally sessile or more rarely pedunculated, may be umbilicated. The whole of the peritoneum may be infected, but the omentum, the mesentery, and Douglas’ pouch are the regions

<sup>1</sup> *Amer. Jour. Med. Sci.*, 1903, cxxvi, 269.

<sup>2</sup> *Lancet*, London, 1905, i, 1047.

<sup>3</sup> *Ibid.*, 1907, i, 1342.



most frequently affected. When the growths are miliary the peritoneum may be otherwise normal, but in most cases the peritoneum shows chronic fibrotic changes resembling tuberculous peritonitis, the white nodules being surrounded with fibrotic thickening and often outlined by a rim of pigmentation. From the resulting contraction the omentum may become rolled up and the mesentery markedly shortened. The intestinal tract may be much shortened, the intestinal walls thickened, and the lumen narrowed. The diaphragm may be much thickened from growth, and in these cases miliary carcinomatosis of the pleuræ with effusion may result. Adhesions may give rise to loculated ascites. In some instances acute or subacute peritonitis is found at autopsy. From implication of the receptaculum chyli or of the thoracic duct the lacteals may be dilated, and from leakage true chylous ascites result; chyloform ascites is commoner.

Occasionally large colloid growths are met with. More than one condition has been described as "colloid cancer" of the peritoneum; secondary growths due to a primary carcinoma of the stomach or colon are occasionally seen, but some of the cases formerly described as colloid cancer are probably primary retroperitoneal growths derived from the Wolffian bodies and are myxosarcomatous or endotheliomatous in nature. The histological character of the tumors will vary with that of the primary growth, spheroidal-celled carcinoma being the commonest form.

**Symptoms.**—These come on gradually with loss of vigor, flesh, and appetite, and, except that they point to the abdomen, are somewhat indefinite. The symptoms vary since they are partly due to the primary growth, which is also usually in the abdomen, and partly to the peritoneal metastases; in fact, it is usually impossible to assign the symptoms exclusively to one or other cause. In addition to the progressive wasting and weakness there may be varying degrees of abdominal tenderness. Pain, on the one hand, may be almost absent, or, on the other hand, there may be colic from obstruction to the lumen of the colon, induced either by a primary carcinoma or by pressure or contraction exerted by secondary growths in the neighborhood. Tenderness and pain may be due to attacks of local peritonitis in connection with the growths.

**Physical Signs.**—In most cases there is ascites which may obscure the existence of any growths. The fluid may be clear, turbid, blood-stained, chylous, or pseudochylous. The abdomen may be much distended. There may be prominent veins under the skin of the abdominal wall. The umbilicus may be infiltrated with secondary growth, and small nodules may be felt in the line of the falciform ligament; it should be remembered, however, that small masses of fat in this position may imitate nodules of secondary growth. As the result of distension the skin of the abdomen shows lineæ albicantes. Even when not previously stretched the skin may from loss of its elasticity be thrown into numerous wrinkles and become somewhat harsh and rough. In a case without ascites, under my care, numerous and extensive lineæ albicantes appeared on the back in the last ten days of life.<sup>1</sup>

<sup>1</sup> *Brit. Med. Jour.*, 1908, i, 494.

Although there is usually emaciation, and to a greater degree than in primary malignant disease of the peritoneum, there is sometimes a very considerable amount of subcutaneous fat. Cutaneous pigmentation is not uncommon; and in very rare instances the skin of the abdomen shows a warty pigmented condition called *acanthosis nigricans*. *Œdema* of the feet, which may creep up the thighs to the abdomen, may be due to pressure on the inferior vena cava, or in the later stages depend on cardiac weakness. In some cases definite tumors can be felt through the abdominal wall; very frequently the omentum is rolled up and palpable as a hard tumor or transverse ridge, which must not be mistaken for the lower margin of the liver. There may be friction over the tumors. Often when ascites is considerable no growths can be detected until the abdomen has been tapped, and when the growths are small nothing may be felt even then. There may be concomitant pleural effusion on one or both sides due to intrathoracic infection. The duration of the disease is seldom more than six months and is often much less.

**Diagnosis.**—When definite tumors can be felt in a patient who has malignant disease of the stomach, colon, etc., there can be no doubt. When tumors are palpable, but there is no history or definite evidence of malignant disease, the diagnosis must be made from tuberculous peritonitis, from fecal accumulation, and from the rather rare condition of multiple hydatids in the peritoneum. Tuberculous peritonitis is commoner in children and women, and may be accompanied by fever and by signs of suppuration about the umbilicus, while injection of the ascitic fluid into guinea-pigs would provide evidence of tuberculosis. Injection of tuberculin into the patient is another means of diagnosis. A blood-stained effusion is in favor of malignant disease. The discovery of multiple tumors in the abdomen should always suggest the possibility of fecal accumulation, and the effects of purgatives and repeated enemas on the position of the tumors should be tested. Multiple echinococcus cysts in the abdominal cavity run a slow course as contrasted with malignant disease, and may be definitely recognizable as cysts, while the history of a hydatid cyst in the liver makes the diagnosis of a similar condition in the peritoneum highly probable. In cases with marked ascites the presence or absence of tumors cannot be settled, and it may be impossible to decide whether the underlying condition is malignant disease or hepatic cirrhosis, simple chronic peritonitis, and other causes of ascites, such as portal thrombosis, until the abdomen is tapped. It should be remembered that the malignant growths in the peritoneum may be too small to be felt. In these cases enlarged glands in the groins or above the left clavicle, and to a lesser degree a blood-stained ascites, indicate malignant disease.

**Prognosis** is, of course, hopeless.

**Treatment** is purely palliative and in the direction of the relief of pain by opium, morphine, and external applications to the abdomen, in the alleviation of gastro-intestinal symptoms, and the removal of ascitic fluid by tapping. To prevent reaccumulation of fluid after tapping, the injection of a dram of adrenin (1 to 1000) diluted with water to half an ounce may be tried.

## CHAPTER X

### SPLANCHNOPTOSIS. VISCEROPTOSIS. ENTEROPTOSIS. GLÉNARD'S DISEASE

By THOMAS R. BROWN, M.D.

THE word enteroptosis, from the Greek words *ἐντερον* and *πτῶσις*, although in reality meaning a falling or descension of the intestines, has been generally used to signify the descent of any or all of the abdominal viscera. The better word, however, is *splanchnoptosis*. In describing the displacement of the individual organs special terms are used, such as *nephroptosis*, to signify descent of the kidney; *gastroptosis*, of the stomach; *splenoptosis*, of the spleen; *hepatoptosis*, of the liver; *coloptosis*, of the colon; while some of the more modern writers on the subject use the term *enteroptosis* to mean descent of the intestines. The condition may be either partial or universal, and the different organs may be affected in varying degrees. It is also known as Glénard's disease, from the physician who first described it carefully. Etymologically speaking, all the terms are incorrect, and we should use *nephroptosis*, *gastroptosis*, etc., as A. Rose has specially insisted.

One thing must be remembered in the discussion of this disease, and that is, that in the earlier days *nephroptosis*, being much more easily recognized, was regarded as the most important feature, and to it were ascribed the protean symptoms often met with, while later investigations with better methods of diagnosis have shown that the displacement of the kidneys is usually associated with the displacement of the stomach, intestines, etc., and that many of the symptoms originally ascribed to floating kidney are in reality referable to displacement of other organs.

**Anatomy and Embryology.**—Before discussing the etiology of *splanchnoptosis* it will be advisable to call attention briefly to the anatomy and embryology of the abdominal organs. These viscera are held in their positions by a number of different forces: by the negative pressure of the thoracic cavity acting through the diaphragm; by ligamentous, vascular and peritoneal attachments; by the pressure of other abdominal organs; and by the supporting power of the abdominal muscles. Physiologically, no organ is absolutely fixed, but each is capable of a slight degree of movement, which may be caused by various factors, such as the position of the patient, the amount of food ingested, the passage of urine and feces, the respiratory and circulatory movements, and pregnancy. Thus we must not consider the abdomen to be filled with viscera that are normally fixed in their positions, but rather of organs capable of a slight degree of movement under a variety of conditions, the only fixed area in the abdomen being the *radix mesenterica*.



Embryologically the subject is interesting because of the fact that a number of authors regard splanchnoptosis as a reversion of the abdominal organs to the embryonic type, as Rosengart and Henle have shown. From the fetal position of the viscera the position found in normal children and adults is produced by gradual ascension of the various viscera, this being largely due to the fact that after respiration the liver rotates and rises into the dome of the diaphragm, and also undergoes a relative diminution in size. In advanced cases of splanchnoptosis the position of the abdominal organs very closely resembles that seen during embryonic life.

**Pathogenesis.**—As regards the pathogenesis of splanchnoptosis divergent views are held, some believing that the condition is congenital, others that it is acquired, while others hold a middle ground. According to Glénard, the starting-point of the condition is the falling of the right colic flexure, due to a weakening of the hepatocolic ligament. This may follow injuries, pregnancies, strains, dyspepsia, typhoid fever, appendicitis, or localized peritonitis, but is primarily due to a constitutional defect as regards the strength and supporting power of the mesenteric tissues which is present in certain individuals.

Stiller is another firm adherent of the congenital origin of splanchnoptosis, and he believes that this inherited tendency is shown by a constant organic type, a slender skeleton, a long thorax, soft, flabby muscles, and a diminution of the panniculus adiposus, and that in these patients may be found a neurasthenic stigma, the floating tenth rib. According to him the basis of the disease rests upon an embryological defect, and the numerous causes which many authors give for this condition are in reality not primary causes, but simply factors which bring about a condition to which the body is already embryologically committed. Fuhs is also a firm believer in the costal stigma, and calls attention to the frequency of splanchnoptosis among young unmarried Swedish girls who have never worn corsets and who have strong abdominal walls. The condition is also found frequently among Arab women, who also wear no constricting articles of clothing. Mathes believes that splanchnoptosis is a constitutional and hereditary anomaly of the entire organism, a lack of vital energy of all the vital tissues, while Harris, who has paid special attention to the etiology of nephroptosis, believes that this occurs in women with a particular body form, which can be expressed mathematically in terms of certain body diameters, and that practically all women with this body form have movable kidneys to a greater or less extent.

Landau believes that the primary cause is a weakness of the abdominal wall, in many cases congenital, while according to Bouveret, neurasthenia is primary, splanchnoptosis secondary. Rosengart believes that in many cases there may be a real persistence of the fetal condition. Riegel, on the other hand, is a firm believer in the acquired nature of the disease, and thinks that any condition which either increases the pressure above the diaphragm or diminishes the pressure below may produce splanchnoptosis, such as pregnancy and parturition, wasting diseases, and the removal of abdominal tumors or ascitic fluid.

Wolkow and Delitzen have carried out a number of interesting experiments in regard to the production of nephroptosis, and they conclude that the use of a belt may dislocate the kidney downward, may fix it, or may even move it upward according to the position of the belt. According to these investigators, nephroptosis is an infallible index of an existing alteration of the intra-abdominal equilibrium. Janovski, from his experimental studies, thoroughly agrees with these conclusions, while Longyear believes that the ligamentous union of kidney and colon is an even more important factor in the etiology of nephroptosis.

Vietor believes that the fundamental cause of splachnoptosis is the inability of the abdominal walls to resist the weight of the viscera, that this is an inevitable accompaniment of the upright position, and that anything which increases the instability of the body will tend to produce this condition, such as marked straightening of the thorax at its lower extremity, marked anterior convexity of the lumbothoracic segment of the spine, and marked tilting forward of the pelvis.

Quincke gives three causes of splachnoptosis: (1) Relaxation or stretching of the abdominal wall; (2) change in the form of the abdominal cavity; (3) stretching of one or more of the suspending ligaments; while Langerhans recognizes five causes: (1) Relaxation of the abdominal muscles; (2) hereditary predisposition; (3) pressure of clothing, as tight belts and corsets; (4) chlorosis; (5) nervous dyspepsia.

The most valuable contribution to the pathogenesis of splachnoptosis is that of Keith, who believes that the condition is the result of a vitiated method of respiration. According to him the organs within the thoracic and abdominal cavities are poised between the muscles of inspiration and expiration, two contending sets, which throughout the life of the individual strive for the mastery. The reason that the right kidney is so much more frequently displaced than the left is because the liver acts directly on the latter, while in the case of the former there is a safety valve in the shape of the splenic flexure of the colon, which may enter or leave the hypochondrium with the greatest freedom; also the left kidney is bound to the spleen, and the fundus of the stomach represents a much lighter hammer than the liver. The adhesion of the base of the pericardium to the diaphragm, peculiar to man and the anthropoids, is a most effective aid against ptosis. Briefly speaking, Keith's conclusions are as follows: (1) The contraction of the diaphragm is the factor which produces the displacement of the viscera in splachnoptosis or Glénard's disease, and further, that of the various parts of the muscle, the crura are the most important agents in producing this result. (2) Before the displacement can be produced, either what he terms the thoracic supports of the diaphragm must have yielded, or the antagonistic abdominal muscles must have been hampered or weakened in their action, as, for example, by tight corsets. (3) The bonds which fix the viscera to the walls of the abdomen are of quite subsidiary importance.

Thus the theories regarding the pathogenesis of splachnoptosis may be broadly placed in three groups: (1) The condition is congenital, and is due to an inherent weakness of the tissues which support the abdominal viscera; such factors as clothing, trauma, disease, etc., are

not the primary causes, but simply contributory ones, which bring out or accentuate the inherited tendencies. (2) The condition is due to a number of conditions, each of which has as its result the weakening of the various visceral supports, due in some cases to pressure, in other cases to adhesions, in other cases to trauma, and in still other cases to a marked diminution of the supporting power of the abdominal wall. (3) That each of the foregoing may be the primary cause of the condition; in other words, that there may be both an acquired and a congenital form of splanchnoptosis.

In the great majority of instances, according to personal observations, the condition is due to a congenital defect, yet in some it may definitely be of the acquired type.

**Frequency.**—In discussing the frequency of splanchnoptosis we will naturally and necessarily quote from the tables of the frequency of displaced kidney, displaced stomach, displaced liver, etc., because in the vast majority of cases the descension of one organ is associated with that of other organs as well, although for various reasons the one organ alone has been considered. Naturally the only tables of real value in this connection are those of recent years, when the condition has been well recognized, and when clinicians have been on the alert to diagnose it. Lawson Tait stated that there were no movable kidneys, and yet we have but to look at many of the older pictures, notably Botticelli's women and Memling's Eve, to realize that the condition has unquestionably been present for a long time, although it is highly probable that it is on the increase. The condition has been found in practically all the races in which it has been carefully looked for, and cases have been described quite frequently among the Arab women and other tribes among whom tight clothing is unknown.

Glénard reported 148 among 1310 patients at Vichy; Stiller meets from 300 to 400 cases of splanchnoptosis in his private practice every year; while Kuttner found 100 cases of this condition among 4000 patients in Ewald's clinic; Kuttner also states that he frequently found floating kidneys in children, which is also the writer's experience and that of Blum. Einhorn in one year saw 70 cases of splanchnoptosis among 1080 males, and 277 cases among 832 females. Of 240 cases of enteroptosis proper, 20 were in men and 220 in women, and in these cases movable kidney was met in 212, movable liver in 23 cases in association with movable kidney, and in 12 patients without movable kidney. Enteroptosis alone was met with in 15 patients, 1 male and 14 females, and movable kidney alone 57 times, 21 males and 36 females. Thus in Einhorn's practice, which is largely devoted to digestive disorders, and in which, therefore, the figures are extremely high, ptoses of the abdominal viscera are met with in 6.5 per cent. of the males and 33.25 per cent. of the females.

As regards the incidence of *movable kidney* the older anatomists and clinicians noted it but rarely; thus, Ebstein found movable kidney only 5 times in 3658 postmortems, while Landau reports only 4 cases among 6999 hospital patients.

The reports of later years, however, show the great incidence of this



condition, especially among women; thus, Lindner found that one out of every four women had displaced kidney; Mathieu found 85 cases among 306 patients; Larrabee reports 112 cases among 272 patients in the Out-patient Department of the Boston City Hospital; Glénard, in his statistics published in 1893, found 481 cases of floating kidney among 3788 patients, 2.7 per cent. in men and 22 per cent. in women; Wolkow and Delitzen found 66 cases among 221 women; Einhorn found nephroptosis in 1.81 per cent. of males and 20.6 per cent. of females. According to Burnam, who has carefully investigated the records of the Johns Hopkins Hospital, one out of every 5 women had a movable kidney, and one out of every 50 men, these figures agreeing absolutely with those of Tuffier.

As regards the grade of displacement, Glénard describes four degrees: (1) When the lower portion of the kidney can be felt only during deep inspiration; (2) when the greater portion of the kidney can be felt, but the upper border cannot be made out; (3) when the whole kidney can be palpated during deep expiration; and (4) when the entire kidney can be palpated, and is capable of being moved about the abdominal cavity, this latter being the true floating kidney. According to Ewald and Kuttner, the degrees of displacement are: (1) The kidney shows a demonstrable respiratory movement without being dislocated to any extent; (2) the kidney shows a dislocation of the first degree, that is, we are able to palpate from one-third to two-thirds of the organ, which can be moved by means of the hand, and is more or less dislocated forward; (3) the kidney shows a dislocation of the second degree, that is, is palpable over its entire extent, is easily moved by the hands and during respiration, and lies near the anterior abdominal wall, or, at least, is easily brought there; and (4) the kidney is dislocated and fixed in an abnormal position. In Kuttner's and Ewald's series of 79 cases associated either with dilatation or displacement of the stomach, in 47 the right kidney was displaced, in 7 the left kidney, and in 25 both kidneys; 18 cases fell under the first grouping, 64 under the second, 19 under the third, and 3 under the fourth.

As regards *age*, displaced kidney, as well as ptoses of the other viscera, is frequently met with in very young children, in several cases under three years of age. In Kuttner's series of 326 cases, 6 were found between one and ten years, 32 between ten and twenty, 82 between twenty and thirty, 123 between thirty and forty, 49 between forty and fifty, 26 between fifty and sixty, and 8 between sixty and seventy; that is, the great majority of these patients when seen by the physician for the first time are between twenty and fifty years of age. Blum has recorded many cases among children, and we have noted the condition frequently in very young infants.

As to the relation of pregnancy to floating kidney, in Kuttner's series of 94, 40 patients had never borne children, 10 had borne one child each, and 44 had borne two or more children each. In Landau's series, 31 of 34, on whom notes were made, had borne no children, while in Lindner's series of 75 patients, 24 had never been pregnant, 12 had been pregnant once, 30 had been pregnant two or more times, while of the others no

notes were to be found. Of Drummond's 27 women patients 16 had borne children, while of Larrabee's 112 cases, 51 were nulliparous and 50 multiparous.

As regards the frequency with which right, left, and both kidneys are affected, in Kuttner's series of 727 cases, in 553 the right kidney alone was movable, in 81 the left kidney alone, and in 93 both kidneys. In Einhorn's series the right kidney alone was movable in 77.3 per cent. of the cases, the left kidney alone in 2.1 per cent., and both kidneys in 20.6 per cent.

As regards the incidence of *gastroptosis*, figures are of little value because, in the first place, the condition is generally overlooked unless associated with gastrectasis or unless special examination is made either by inflation or the use of the *x*-rays, and in the second place because many of the symptoms, which in reality were due to a displacement of the stomach, have been ascribed to displacement of the kidney and treated accordingly. Kuttner and Ewald report 100 cases of displaced kidney, 94 in women, 6 in men, in 79 of which there was either a dilatation or displacement of the stomach. The writer's experience has been that in almost all the cases of splanchnoptosis the stomach is involved to a greater or less extent. The subject is still somewhat undecided because of the great difference of opinion as to the normal position of the stomach.

Glénard has reported 51 cases of *displaced liver*, 32 being associated with movable kidney, and of these, 30 were women and 2 men. Einhorn reports 21 cases of displaced liver in 369 women, 9 cases in 439 men; a moderate degree of abdominal flaccidity was present in 16 of the 21 women. Graham has collected 68 cases of displaced liver, 55 in women, 13 in men, and Savelieff has recently collected 118 cases from the literature.

Several isolated cases of *floating spleen* have been reported, although, unless the spleen is markedly displaced, a ptosis is difficult to determine, because of its position, which can only be determined by the most careful percussion and because of the absence of symptoms. The frequency of displacement of the *pancreas*, of the *colon*, and of the *sigmoid flexure* is difficult to determine. The displacement of the pancreas is of interest because Glénard's *corde colique transverse*, which he believed to be the constricted transverse colon, Ewald regards as the pancreas.

*Cardioptosis*, or the descension of the heart, has been described in a few cases. Einhorn found it 22 times in 926 patients, 18 men, 4 women, and in about one-half of these cases there was an associated hepatoptosis. He thinks the condition is probably due to the downward displacement of the diaphragm. Abnormal position of the œsophagus and cardio-spasm have been noted in a certain number of cases of gastroptosis.

The association of displacements of the pelvic organs with splanchnoptosis is a subject to which very little attention has been paid, and yet it is one of extreme importance, because retroflexion of the uterus is a very frequent accompaniment of displacement of various abdominal organs. Smithwick found that of 34 women with splanchnoptosis, 80 per cent. had retroversion of the uterus generally in a marked degree.

**Symptoms.**—We will discuss the symptomatology of splanchnoptosis in general, and later call attention to the symptoms especially referable to each of the displaced organs. In the first place, it must be insisted upon that there may be absolutely no symptoms whatsoever, and, in the second place, that the intensity of the general symptoms does not, as a rule, depend so much upon the extent of the displacement of the various viscera as upon the degree the nervous system is involved. In this connection we must not forget that all of these symptoms have been ascribed in turn to each of the viscera, according to whether kidney, stomach, liver, or intestines were the special object of study, and yet that in the vast majority the symptoms are referable to a displacement of all or most of the viscera, although the degree of displacement may be different. The usual picture of a case which presents symptoms is that of a thin, pale young woman or man of slight build, with dyspeptic and nervous complaints, a nervous expression, and thin, soft abdominal walls in which there is a marked lack of tone. Some have called attention especially to the juvenile expression of the face, others to the fact that the picture closely resembles that met with in phthisis. We may have symptoms of the most aggravated type of *neurasthenia*, to which are added various abdominal symptoms, such as indigestion, constipation, pain in various portions of the abdomen, a feeling of lack of abdominal support, frequent, sometimes painful, urination, backache, sideache, various respiratory symptoms, cardialgia, pain during or after meals, sometimes nausea and vomiting. All of these symptoms are aggravated by standing, walking, or exercise, while the prone position causes them to markedly diminish and sometimes to disappear for the time being. It is also noteworthy that the symptoms become less if the abdomen is lifted up either by an artificial support or by the hands of the physician as he stands behind the patient—the so-called “belt test” of Glénard—or after elevation of the foot of the bed. The greater the congenital anomaly, and the earlier the adjuvant factors act upon one so predisposed, the sooner will these symptoms make their appearance. Among the more important objective symptoms may be mentioned a flattened abdomen, often with hypoplastic walls, a bent spinal column, sometimes an abdomen flattened in the epigastric region but distended below the level of the umbilicus; sensitiveness to pressure near the tenth rib in some cases, a cord-like transverse colon (or displaced pancreas, according to Ewald), through which the pulsation of the aorta can be distinctly felt; while in some cases visible swellings can be seen in abnormal locations due to displacement of the various viscera.

Glénard divided the symptoms into three special groups: hypostasis, or lack of tone of the abdominal walls, splanchnoptosis, and enterostenosis. The first shows three special symptoms: deformity of the abdomen, flabbiness of the abdominal walls, and the ease with which the hypochondrium can be compressed. *Splanchnoptosis* shows four special signs: splashing sounds in the stomach, epigastric pulsation, floating kidney, and ptosis of the transverse colon. *Enterostenosis* has three special signs: palpable contracted band of the transverse colon, of the cecum, and of the sigmoid flexure.



Other symptoms of the most protean character have been ascribed to this condition. Meinert believes that chlorosis in young girls is sometimes a crisis of splanchnoptosis, while Quinke puts stress upon the respiratory symptoms, such as shortness of breath on standing or after exertion, cardiac oppression or distress, and sometimes dizziness or weakness.

Glénard himself describes four forms of splanchnoptosis, the gastrointestinal, the lithemic or hepatic, the neurasthenic, and the cachectic, and believes that in many cases the patient goes from one form into the other in the order named. Keith, who has paid so much attention to the respiratory phenomena of splanchnoptosis, calls special attention to the frequency with which cervical curvature or ewe-neck is met. He believes that from a clinical point of view the most important of the visceral bonds is the gastrohepatic omentum, and that more than half the results of ptosis of the liver and stomach are due to compression, straining or distortion of the bile, blood, nerve and lymph channels contained in this omentum, and that gall-stones are commonly present in cases of splanchnoptosis.

As to the relationship between neurasthenia and splanchnoptosis, there is a marked difference in opinion, some holding that neurasthenia is primary and splanchnoptosis is secondary, others the reverse, while a third group holds, and probably rightly, that in most cases each represents a congenital fragility of tissue independent primarily of each other, but frequently associated and reacting very deleteriously upon each other.

It must strike our gynecological brethren that the symptoms which they have ascribed to retroflexion of the uterus bear a striking resemblance to those of splanchnoptosis, and this accentuates the fact already noted that in the vast majority of cases retroposition and retroflexion of the uterus are but associated signs of a general splanchnoptosis, and to expect relief by a ventral fixation of the uterus seems chimerical.

**Gastroptosis.**—Gastroptosis, although one of the less frequently recognized of the visceral ptoses, is one of the most important as regards symptomatology. Undoubtedly many of the symptoms referred to displacement of kidney or liver are in reality due to an unrecognized displacement of the stomach. As to its frequency, it is being more and more recognized as it is being more carefully investigated. Meinert finds displacement of the stomach in 80 per cent. of the patients in his gynecological clinic, while Thompson, who has noted many cases, finds it six times more common in women than in men.

In the downward dislocation of the stomach we have two main forms: First, the whole stomach may be dislocated downward, and second, the stomach may occupy a more vertical position, although, strictly speaking, the former is rare, due to the firm fixation of the cardiac end. The most frequent form is the subvertical, the next is the vertical, while the loop, crescent, or garland form is less common. The vertical or subvertical forms are peculiarly liable to dilatation, this being, of course, aided by a general weakness of the patient, frequent overloading of the stomach, relaxation of the abdominal wall, pregnancy and parturition,

rapid loss of weight, and constriction due to corsets. As regards symptoms, there may be none whatsoever; in fact, the symptoms directly referable to the stomach are largely dependent upon the associated dilatation of the motor or secretory anomalies. Steele and Francine found some dilatation of the pyloric extremity in each of 70 patients examined by them. We must, therefore, regard the symptoms met with in gastropotosis as largely due either to a perversion of the motor or the secretory powers of the stomach, or to a dilatation with its characteristic symptoms due to the retention and decomposition of food, and the associated toxemia. If the ptosis is marked, it is hard to see how it is possible to prevent difficulty in the propulsion of food, leading to increased fermentation in the stomach and subsequent distension and atony. So long as the stomach is not overtaxed there is little or no distress, for if the ptosis is not great the stomach is easily able to perform the additional amount of labor. If, on the other hand, excessive work is thrown on the stomach, as after very large meals, rapid eating, the ingestion of much easily fermenting food, or the upright position after eating, the stomach is unable to do the excess of work, and dilatation occurs.

The *symptoms* which are especially referable to the displacement of the stomach are distress and flatulence after meals, sometimes nausea and vomiting, tachycardia, anorexia, coated tongue, numbness and dizziness, pain, which may be due either to fermentation, associated catarrh, increased acidity, or the pressure of the displaced stomach on the solar plexus, and a feeling of lack of support, while in some cases the dread of gastric disturbances leads to slow starvation and cachexia. Many of these symptoms are, of course, in the main due to the associated dilatation or motor insufficiency, while in all cases the quantity of food seems to be of more importance than its quality in the production of symptoms. Rose believes that the condition is identical with atonia gastrica. A splashing or a rumbling sound in the stomach is frequently met with. Of course, it must be remembered that in many cases the symptoms are more referable to the neurasthenia so frequently associated with this condition than to the displacement of the organ *per se*. In gastropotosis, as in the other ptoses, the symptoms are usually lessened by the prone and increased by the upright position.

As to the effect of ptosis upon the gastric secretion, subacidity is the rule as shown in patients examined by the writer; as the dilatation became more marked the free hydrochloric acid diminished, and was absent in most of the patients with very high grades of dilatation. Steele and Francine, from a study of 70 cases, also found that diminution of free hydrochloric acid was the rule.

**Nephroptosis.**—Of all the divisions of splanchnoptosis, nephroptosis, or displaced kidney, has absorbed by far the greatest amount of attention and study, an unfortunate condition in many ways, because to it have been ascribed many of the symptoms which undoubtedly are referable to the displacement of other organs. Some, such as Israel, Litten, Morris, and Kuttner, believe that the so-called first degree of displacement of the kidney is not pathological. Harris, who is a firm believer in the congenital origin of nephroptosis, and who found a movable tenth

rib in 61 of 110 cases, believes that the characteristic sign is a peculiar body form, a marked contraction of the lower end of the middle zone of the body, with a diminution of the capacity of this portion of the body cavity. Becker and Lenhoff divide the distance from the suprasternal notch to the upper edge of the symphysis pubis by the least circumference of the abdomen, for the sake of convenience, multiplying this by 100; the average index was 77, and they found that if it was above 77 the kidneys could usually be left, while if below 75, as a rule they could not be felt. Albarran, Sheldon, and others, have noted numerous cases in the same family.

Among *symptoms* definitely referable to the kidneys themselves may be mentioned a feeling of lack of support in the back and flank, frequent urination, associated with burning sensations, which is sometimes diagnosed and treated as cystitis, and pain which may be either continuous or intermittent, and which is often relieved by the patient lying down. There may be intermittent hydronephrosis with polyuria after the reduction of the kidney to its normal position, the so-called *Dietl's crises*, consisting of paroxysmal attacks of intense pain, nausea, and vomiting, according to some due to intermittent hydronephrosis, according to others to torsion of the renal vessels and nerves. Blood, albumin, and casts may occur in the urine. Some believe that the displaced kidney produces and maintains a congestion of the pelvic organs. Some patients complain of feeling a moving mass in the abdomen, others have definite symptoms of sciatica and crural and intercostal neuralgia. Intermittent hematuria and nephritis have been described, while in two cases of post-operative pyelitis examined by the writer the fact that the affected kidney was in each case the displaced organ suggests that its resistance is lowered by the displacement.

Burnam, from his study of the cases of nephroptosis in the Johns Hopkins Hospital, finds that only one case in ten of movable kidney has marked local symptoms, the cardinal symptoms being pain in the side, gastric symptoms, and nervousness. The dragging dull pain in the flank is about three times as common as acute attacks of Dietl's crises. About one out of every eight cases with Dietl's crises shows a beginning hydronephrosis, about one out of every three cases shows marked gastric symptoms, and one out of every three cases shows pronounced nervous symptoms. Tuffier believes the gastric symptoms in nephroptosis are due to an atonic gastric dilatation, while of the paroxysmal pains in the renal region he describes two kinds: first, slight pain followed by the passage of much clear urine, and second, the pain associated with intermittent hydronephrosis, a renal tumor usually being made out during the paroxysm, while the amount of urine, which is markedly diminished with the onset of the pain, is often markedly increased with its subsidence, part of this increased flow being due to reflex stimulation of the healthy organ. Kelly, by catheterization of movable kidneys, has shown that a slight hydronephrosis is the rule, for he found the average capacity of the renal pelvis in 65 cases of nephroptosis to be between 12 and 13 cc., the normal capacity being 7 to 8 cc.

The relationship between nephroptosis and dilatation of the stomach



has not as yet been definitely determined. According to some the gastrectasia is definitely secondary to gastropptosis, while according to others the displaced kidney plays a very important part in the production of the dilatation. It seems probable that the dilatation of the stomach so frequently met with in splachnoptosis is in the vast majority of cases etiologically dependent upon the gastropptosis, and that there is no causal relationship between it and floating kidney except in very rare instances. There is no question but that chronic appendicitis is frequently associated with displaced right kidney. Many have also called attention to the relationship between floating kidney and obstruction of the common bile duct.

**Hepatoptosis.**—Floating liver is frequently not diagnosed, due partly to the difficulty in making out a moderate degree of displacement, partly because it is frequently regarded as an enlarged liver and partly because by the vast majority of observers the kidney is the only organ carefully investigated in splachnoptosis; yet the tables of Graham, Einhorn, Landau, and others show that the condition is not rare. The *symptoms* of the condition are rather indefinite. There may be spontaneous pain, which is sometimes brought on by jumping, walking, raising the right arm, sneezing, coughing, and yawning, while sometimes paroxysms of pain occur without apparent cause. In the writer's experience pain has been a very common symptom, usually relieved by making the patient lie on the back or on the right side, or by manual replacement of the organ. The pain is commonest in the right hypochondriac and epigastric regions, radiating thence toward the shoulder or the flank. Pressure, although rarely painful, often produces peculiar sensations in various portions of the body, especially the arms and shoulders.

Many patients complain of digestive symptoms, meteorism, constipation, or of feeling a movable body, colicky pains, respiratory disturbances, palpitation and jaundice. Keith believes that they are caused by the compression of the bile, blood, nerve, and lymph channels contained in the gastrohepatic omentum and that gall-stones are very commonly associated. Steele showed by experiments on a cadaver that biliary obstruction is met with in floating liver, pressure in the common duct being between two and three times the normal. Landau describes three grades of hepatoptosis: (1) moderate descent with anteversion or retroversion; (2) marked descent either with lateral displacement toward the right, or with anteversion or retroversion; (3) vertical or oblique displacement, the left lobe descending into the abdominal cavity.

**Descent of the Intestines.**—This is practically met with in every case of splachnoptosis, but the difficulty of making a definite diagnosis has made most observers minimize its importance, yet the intestinal symptoms are many and diversified, and among them may be mentioned constipation, fermentative dyspepsia, mucous colitis, which is quite common, various symptoms due to stenosis of the intestines, marked fulness in the lower half of the abdomen, and peristaltic movements in the displaced intestines, often made out if the abdominal wall is thin. Ewald believes that the intestinal disturbances are due to the dragging of the bands on which the sections of intestines are hung, producing

reflex irritation of the intestines, disturbances in their circulation, their motor and secretory functions, while, due to the sinking of the transverse colon, the horizontal portion of the duodenum is pulled downward. It is possible that a low grade of peritonitis may develop from the persistent fecal stasis, and that this may be the cause of Lane's band, Jackson's veil, etc. The small intestines, containing liquid feces, are but slightly affected by ptosis, but in the large intestines, containing solid feces, a loop or kink is of much more serious importance and may produce marked constipation and possibly the symptoms of auto-intoxication. A kinked or a redundant sigmoid is often the cause of most intractable constipation.

**Descent of Spleen and Pancreas.**—The descent of the *spleen* has been rarely described, because it is difficult to recognize slight displacements and because symptoms are usually absent. In a few cases which have symptoms the patients complain of dragging, uneasy sensations in the back and side. All grades of splenic displacement have been described, while the fact that several cases have been found in members of the same family suggests a congenital origin. The organ is usually enlarged, while sometimes torsion of the pedicle may occur with gangrene.

As regards the *pancreas*, we must remember that a segment of this organ is firmly bound to the radix mesenterica, and is, therefore, fixed, but Ewald believes that the other portion may undergo descension, and may be felt as a constricted cord, which Glénard believed to be the transverse colon.

**Diagnosis.**—The diagnosis of splanchnoptosis should be easily made by all careful observers. It can often be made when the patient is first seen; the characteristic body form, the expression frequently described as juvenile, the evident neurasthenic tendency so frequently associated with splanchnoptosis should at once call our attention to the possibility of this condition. Harris, Becker, Lenhoff, and others have expressed this peculiar body form mathematically, and the measurements which can be made in a few moments are often very suggestive. Others insist on the importance of a floating tenth rib in this condition. In all cases the vague and protean symptom-complex of nervous and digestive disorders, inability to do hard mental or physical work, and the other symptoms which have been described should make us suspect the condition. We must remember, however, that many patients show no symptoms whatsoever, and in such the diagnosis can only be made by a careful physical examination.

As regards the diagnosis of *gastroptosis*, splashing or succussion sounds are frequently heard, there is commonly a sinking in of the epigastrium, with a bulging in the region of the umbilicus or below it, while if the abdominal wall is thin peristaltic waves may occasionally be definitely seen. To exactly diagnose the form and position of the stomach we may attempt to percuss the organ, use auscultatory percussion, or we may with the stethoscope over the stomach determine the length of time it takes for fluid to pass from the mouth into this organ. All these methods, however, are inexact, and it is advisable to distend the stomach; make use of Türk's gyromele; Einhorn's method of gastric

diaphany, an electric light being introduced into the stomach; or inflate the stomach with water. Recently much work has been done in using the  $x$ -rays in diagnosing this condition. The fish-hook, vertical, cow-horn (crescent, half moon), and spasmodic hour-glass forms have been regarded as normal types. Certainly from  $x$ -ray examinations the position of the normal stomach and intestines is lower than that described by the anatomists, this in part, however, being due to the fact that most fluoroscopic examinations of the gastro-intestinal tract are made in the upright position.

In *nephroptosis* sometimes the displaced kidney can be distinctly seen through the thin abdominal wall, while in many cases a sinking in of the flanks can be noted. The only satisfactory way to make the diagnosis, however, is by means of bimanual examination and palpation of the organ. The patient should be examined both in the standing position, lying on the back, and lying on either side, while it is extremely important in many cases to make the patient walk around, hop, jump, or support herself with both hands on the side of the bed before making the examination. Many mistakes have been made by examining patients in bed after a night's rest when the kidney has returned to its normal position. Glénard's *procède de pousse*, the lifting up of the kidney with the fingers and its palpation with the thumb is a simple and easy method of determining displacement of this organ. In the case of *Dietl's crises* a tumor in the lumbar region is frequently made out, which disappears on the cessation of pain. It is an unquestionable fact that too frequent or too severe palpation of the kidneys may harm these organs, and albumin, casts, and blood may be found after such an examination.

In *hepatoptosis* we practically always find a tumor in the right side of the abdomen with its convex surface directed forward. In making the diagnosis we use both palpation and percussion. On percussion the liver dullness, instead of beginning at the fifth rib or fourth or fifth interspace in the mammillary line, is at a much lower level, often the costal margin, while the lower limit of dullness is correspondingly depressed. In place of the normal liver note in the hypochondrium and epigastrium, we meet a tympanitic note due to the ascent of coils of intestine. When the patient is made to lie on his back or his right side with the hips elevated, the liver usually falls back into its normal position, and the topographical percussion is normal. For this reason it is important to percuss first with the patient in the erect position. By bimanual palpation we can make out the characteristic tumor in the hypochondriac or lumbar region; the patient must be examined in both the prone and upright position, and an attempt must be made to replace the organ. Because of the rotation of the organ the liver always seems enlarged. Sometimes by inspection a slight bulging of the abdomen on the right side is made out. We must remember that sometimes replacement is impossible because of adhesions, while in all cases we must differentiate a displacement which is part of a general splanchnoptosis from that due to pleurisy with effusion, diaphragmatic abscess, or from enlargement or tumors of the liver.

In diagnosing displacement of the *intestines*, by far the most satisfactory



method is the use of the *x*-rays, bismuth being given either by mouth or by enema. Usually the cecum and the transverse colon can be palpated as cords, while inspection will sometimes show us peristaltic waves in the displaced coils. By distension through a rectal tube by air or nitrogen gas we can usually determine satisfactorily the position of the transverse portion of the colon. The pulsation of the abdominal aorta can usually be easily felt. The low position of the hepatic and the high position of the splenic flexure, and the fact that the contents appear to remain longer in the cecum than elsewhere have been specially noted in *x*-ray examinations.

The diagnosis of *splenoptosis* is usually easy, as by palpation the organ with its sharp edge and notch may be easily made out. If, however, the organ is fixed in an abnormal position and deformed by adhesions the diagnosis is much more difficult.

If we make use of the methods described above, the diagnosis of splanchnoptosis should be easily made. In women from a careless examination the condition is frequently regarded as a purely gynecological one, while in some cases gastropptosis with the cachexia sometimes associated with it has been mistaken for gastric ulcer or carcinoma. Among the conditions which may be mistaken for floating kidney are fecal tumors in the hepatic flexure or in a loop of the small intestine, a distended gall-bladder, a myoma of the uterus with a long, thin pedicle, or a small ovarian cyst or tumor. Among the conditions for which floating liver has been mistaken may be mentioned renal tumors and hydronephrosis, nephroptosis, and certain rare cases of thickened mesentery or omentum. The spleen has occasionally been mistaken for a uterine myoma, or an ovarian cyst or tumor.

**Prognosis.**—It must be remembered, in the first place, that in many patients no symptoms are present and no treatment necessary. If they are seen early and are willing and able to carry out the prophylactic measures described, or in those cases in which the symptoms are almost exclusively referable to one displaced organ, real success may attend the treatment, be it medical or surgical; but in the majority of cases seen in adult life, when the organs show considerable displacement, the symptoms are marked and varied and the nervous system considerably involved, although the condition may be markedly relieved in many cases and in some the symptoms made to entirely disappear, yet there will be a large number in whom treatment is discouraging.

**Treatment.**—The treatment is in the main rather unsatisfactory, particularly so if the symptoms have been present a long time and the displacement of the various viscera has reached a marked degree. To comprehend the proper treatment it is well to remember that in the majority of cases the condition in all probability depends on a congenital fragility of tissue, while in those so disposed numerous secondary factors may bring about the displacement of the various viscera.

**Prophylaxis.**—To prevent marked manifestations of splanchnoptosis it is most important that the tendency should be recognized early and every possible method of prophylaxis carried out. Children with the characteristic body form, or with a slight displacement of any of the

abdominal viscera, should be treated with the utmost care; they should be made to lie down during certain hours of the day, especially after meals; great care should be paid to their diet, and if they are extremely thin every effort made to fatten them; the strength of the diaphragm, the intercostals, and the abdominal muscles should be increased by carefully chosen exercises; they should be given breathing exercises, in hope of enlarging the lower thoracic zone; sometimes they should be made to wear abdominal bandages for a short period of time if their abdominal muscles show great lack of tone; abdominal massage should be given if possible, and everything should be done to put them and to keep them in the best possible physical condition.

Attention should be paid to all persons, whether adults or children, during and after acute or chronic diseases associated with marked loss of weight or diminution of muscular tone, and one should be most careful about allowing such patients to get up from bed and go back to active occupations. Systematic overfeeding associated frequently with massage should be carried out to bring back body weight and muscle tone to normal. Great care should be taken after rapid obesity cures, and it is probable that in this, as well as in a number of the other above conditions, wearing a bandage for a short period of time would be advisable. Too much care cannot be taken during the puerperium. The patient should not be allowed to get up too soon, and when she does she should be provided with a snug abdominal support until the mechanical conditions within the abdominal cavity approximate the normal again. Great care and practically the same precautions should be taken after the removal of large quantities of ascitic fluid, or of large abdominal tumors, for in these conditions, as in pregnancy, there occurs a sudden diminution of intra-abdominal pressure. It is essential that we as physicians should demonstrate to our patients the dangers from the use of tight corsets or tight belts, and if they insist upon their continuance try to persuade them to wear the less unhealthful kind, that is, the straight front corset, in which the pressure is exerted upon the lower half of the abdomen. The great majority of patients with splachnoptosis are deficient in body fat, and even when no symptoms are present we should advise such patients to so regulate their diet and mode of life that an increase in weight will take place. Patients with this tendency should systematically carry out breathing exercises and other exercises to improve the tone of their respiratory and abdominal muscles.

**General Treatment.**—The diet in splachnoptosis depends largely upon the degree to which the stomach and intestines are involved. Ample nutrition to increase the body weight is most important, and this is best obtained by following a simple mixed dietary with little fluids at meals, while often between meals raw eggs and milk are given; in other cases the patient may be put at first on an absolute milk diet associated with rest. By these methods weight can be added with practically always a marked improvement; we must, however, be extremely careful not to overload the stomach and not to increase the tendency toward dilatation. Often it is advisable to insist that the patient lie down for some time after each meal.

We should advise our patients against wearing tight clothing, and especially against wearing anything that constricts the lower half of the thorax. Great benefit can be derived from carefully selected outdoor exercises and Swedish movements, although these must not be overdone; in fact, it is wise to begin very gently and to gradually increase as the tone of the abdominal muscles improves. Patients should be taught the proper mode of breathing and of standing. Both abdominal and general massage is of real value in this condition. Electricity has been recommended.

It has been frequently observed that after rest in bed, especially with the foot of the bed elevated, these patients often show marked improvement, especially in cases of marked gastropptosis with some dilatation, and a strict rest cure often produces splendid results. In some cases during pregnancy the symptoms are markedly relieved.

Hydrotherapy is often helpful both as regards the gastro-intestinal and the nervous symptoms, and the Scotch douche has been found specially beneficial. In cases of associated dilatation of the stomach lavage is sometimes indicated in association with a careful diet.

**Medicinal Treatment.**—Medicine plays but a very small part in the treatment. For the constipation so frequently present we should first try massage, and perhaps electricity, exercise, diet, and hydrotherapy; if these do not prove effectual, enemata may be given, especially those of oil, while if laxatives are necessary, we may use sodium sulphate and aloes, as suggested by Glénard, or Epsom or Rochelle salt, as suggested by Ewald, or any simple laxative. If anemia is present, iron and arsenic are indicated, although each must be used with care, because they may increase the gastro-intestinal symptoms. As a general tonic nothing is so good as strychnine in increasing doses. As regards water, but little should be taken with the meals, as a rule, but a considerable amount should be taken on waking, in the middle of the morning and afternoon, and at bedtime; the alkaline waters are especially satisfactory. We may give alkalis for hyperchlorhydria, hydrochloric acid and bitter stomachics in subacidity and anacidity.

**Treatment by Mechanical Supports.**—In the hands of most clinicians the use of various mechanical supports in association with the measures already described has proved of great value. The object of the support is to lessen the volume of the lower half of the abdomen and to increase intra-abdominal pressure; to get satisfactory results it is essential that the corset or belt should be applied with the patient in the inclined dorsal position, so that the various viscera are in their positions of least descension. The support is dangerous if it is not well made or applied properly, because if the pressure is above any of the displaced viscera it increases the descension, and unless the patient carries out systematic abdominal exercises the use of the bandage is likely to decrease the tone of the abdominal muscles. As a rule, when its use is associated with the proper dietetic, hygienic, and medicinal measures, a disappearance of many of the symptoms results in the majority of cases.

Many different kinds of bandages have been recommended: Glénard advises an elastic bandage with straps; Rose one made of adhesive plaster; Gallant a corset made to fit the patient and laced from below



upward with the patient in the inclined dorsal position. Ewald and Kuttner use besides the bandage a pad in kidney displacements, Riegel a pad or bolster in gastropotosis, Enriguez a pneumatic pad.

**Operative Treatment.**—It has always been a moot question whether splanchnoptosis is a medical or a surgical condition. It seems that in the vast majority of cases it is strictly medical, and only surgical when the symptoms are so definitely referable to one organ that suspension will offer a good chance of the disappearance of the symptoms; in *every* case hygienic, dietetic, and mechanical measures should be faithfully tried first. Among the indications for surgical interference may be mentioned those cases in which practically all the symptoms are referable to the displacement of one organ. In the case of the *kidney*, Dietl's crises, intermittent hydronephrosis, symptoms suggestive of renal or hepatic colic, more or less constant pain, symptoms due to pressure of the displaced kidney upon other organs, or upon the sympathetic or genitocrural nerves, are all indications for operative treatment; and also, as Kelly has shown, when the attacks of pain may be reproduced by injecting salt solution into the renal pelvis through a ureteral catheter. In the case of the *liver*, pain of a tearing, twisting character if frequent, attacks like hepatic colic, and symptoms due to pressure on other organs, in the case of the *spleen*, torsion of the pedicle with swelling and gangrene, in the case of the *intestines*, constipation which does not yield satisfactorily to any medicinal or mechanical treatment, are all indications for surgical measures. It seems also justifiable to try operative measures in those cases with marked symptoms when all other methods have failed.

In operating upon the *stomach* various methods have been devised. Duret, in 1896, stitched the stomach to the abdominal wall; Lambotte attached by suture the splenic and hepatic flexures to the abdominal wall, thus lifting up the stomach; Webster resected the abdominal wall, bringing together the recti, which had undergone diastasis; Walker performed gastrojejunostomy; Eve operated by placing sutures through the lesser curvature, the lesser omentum, and the liver substance; Coffey by suspending the stomach in a hammock made by the great omentum; Blecher and Bier by shortening and folding the gastrohepatic ligament. Beyea passed sutures through the gastrohepatic and gastrophrenic ligaments, the stomach by this method not being fixed, but elevated into its normal position without affecting its mobility; while in cases of gastropotosis with marked dilatation, gastro-enterostomy or perhaps in some cases pyloroplasty, may be performed. It must not be forgotten that in some of these cases fixation is followed by dilatation, persistent vomiting, and even by marked thinning of the stomach wall.

As regards fixation of the *kidney*, many methods have been described, such as suture through the fatty capsule alone, through the fibrous capsule alone, through the kidney substance, splitting and dissecting the capsule and stitching it to the lumbar muscles, and packing with gauze, which is kept in until firm adhesions form. Most operators advocate suture of the parenchyma in addition to a free dissection of the fibrous and fatty capsule, while Kelly insists upon the Brödel stitch. Wehrmann and Harris believe that the tendency has been to stitch the kidney too high,

as the liver may again press upon the upper pole and bring about a recurrence of the condition. Relapses after nephropexy are due either to this or to insufficient fibrous union between the kidney and the lumbar muscles; in some cases the kidney is fixed in the wrong position and the function of ureter and bloodvessels markedly interfered with; in women a satisfactory nephropexy is peculiarly difficult because of the greater obliquity of the lower ribs.

The mortality in nephropexy is practically *nil*. Burnam finds that the result of the anatomical fixing method is practically perfect, there being no failures if the operation is properly done. As to the results, he found that 90 per cent. were cured of pain, about the same number showed a relief of stomach symptoms, while 50 per cent. were improved nervously; the results where both kidneys were movable were practically the same as in the case of unilateral disease if both were suspended. Tuffier has found that the result of fixation of displaced kidneys when hydronephrosis is present is not so good as in cases in which it is absent, for while the operation relieves the pain, the distension if present for long has affected the integrity of the organ, and it never regains its normal tone. Treves believes from a study of 300 cases that suturing of the kidney should be a rare operation, as he believes as good, if not better, results are obtained by the use of mechanical supports.

As regards fixation of the *liver*, hepatopexy, various operations have been devised and performed. Billroth and others have sutured the liver to the abdominal wall, Langenbech has selected the lower costal cartilages as the points of fixation, some have produced adhesions between the convexity of the liver and the diaphragm by irritation of their surfaces, while others have sutured the fundus of the gall-bladder to the parietal peritoneum. Rovsing has reported 18 hepatopexies with good results. In most cases movable *spleen* requires no special treatment, but with torsion of the pedicle and symptoms of stasis, or symptoms of pressure upon other organs, splenectomy has been done.

In displacement of the *intestines* considerable surgical work has been done recently. In the case of the small intestines, filled with liquid feces, ptosis produces comparatively slight symptoms, but the presence of solid feces in the large intestines means that descension is frequently associated with persistent and intractable constipation, this being especially so in ptosis and kinking of the sigmoid. To counteract this, various operations have been performed, suspension of the sigmoid flexure (sigmoidopexy) and even resection of the sigmoid. Within the past few years resection of the colon as practised by Lane has been frequently done, while appendicostomy and cecostomy or colostomy, with subsequent lavage of the intestine for a long period through the new opening, have been done in the hope of relieving the toxic symptoms present in certain of the cases of very marked enteroptosis, especially those in which many adhesions are present.

# PART II

## DISEASES OF THE URINARY SYSTEM

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### CHAPTER XI

#### INTRODUCTION TO THE DISEASES OF THE KIDNEY

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BEFORE considering in detail the diseased states of the kidney, it is necessary to collate some of the most important facts relative to urinary excretion and the work performed by the several parts of the kidney. Some investigators exalt the importance of the glomerulus, others of the tubule; some believe that forces largely mechanical govern the excretion of urine, others that the vital powers and the selective ability of cells are more potent. As often happens in a discussion in which contraries are dogmatically asserted, there is some truth in both views: most physiologists believe that the urine is produced as the result of carefully coördinated work on the part of the vascular pressure, the secretory powers of the cells and osmotic influences at work between blood, lymph, cell-fluid, and urine.

#### THE PHYSIOLOGY OF THE KIDNEY

Since the days of Bright the importance of the kidney as a seat of disease has certainly not been underestimated, so that there are diseases with urinary manifestations, such as diabetes, in which it is difficult to keep the kidney out of the mental picture, innocent though it be. As an excretory organ, while it probably stands second to the alimentary tract, it certainly surpasses in importance the skin, whose total excretion of water it equals, and it greatly surpasses such subsidiary systems of excretion as the breath and the saliva. With excretion so large and so important, it is natural that it should be held responsible for much that merely goes past its portal; being dependent on other systems to a large extent, the abnormal products appearing in the urine are often not the product of disease of the kidney but of some other organ or system. The kidneys excrete and put the finishing touches upon the urinary fluid; they are acting at the end of the metabolic course both as active and as passive agents. There are some modifications of the excreted products over which they have control, and some over which they have none.



The limits of such control are what we endeavor to determine by experimental work, and there is at our disposal evidence which tends to show that while to some extent the kidneys are mechanical contrivances, mere filters, so to speak, they are to a far greater degree active, specific glands.<sup>1</sup> The daily performance of the healthy kidney is no doubt a combination of these mechanical and vital processes. Yet the more one follows the conflict of evidence and the varying results that have been obtained by the use of similar experiments on kidney functions, the more must it be realized that these functions need not be absolutely hard and fast, unalterable, specific rules of procedure. Glomerulus and tubule assist one another: in time of stress, one may compensate for failure of the other: if both fail together, their work may be temporarily performed, in some degree, by the adjuvant systems, the alimentary canal, the skin and the other lesser excretory organs. Witness in nephritis the excretion of urea in the saliva, of chlorides in the feces. It is obvious that the variations in experimental results, and the difficulty experienced in trying to lay down hard and fast rules as to kidney function arise from this very "give and take" between the different parts of the kidney, and between the kidney and its fellow-organs.

The rules of function that can be fairly considered as settled are these: The glomeruli excrete water and salts, such as sulphates, phosphates, and carbonates, especially when these are in excess; many foreign substances, such as sugar, peptone, egg albumen, and hemoglobin, if injected, are also excreted by the glomeruli; yet sugar is excreted by the tubules when the kidney is poisoned by phloridzin, and many pigments, when injected, have been found to be excreted by the tubules. Urea is so readily diffusible that it is hard to believe that it is not excreted by the glomeruli, yet urea and uric acid are generally credited to the tubules; uric acid, indeed, seems to be thrown out by the convoluted tubules and the ascending loop of Henle, while phloridzin, cantharidin, and perhaps mercury are excreted by the tubules. Apparent discrepancies as to the place of excretion of any substance arise not from mistaken observations, but because the adaptability of the kidney causes these substances to be excreted now in one way, now in another; in short, it seems as if the tubules can share almost every glomerular labor when the need arises.

There is much reason to suppose that water and salts may be excreted by the tubular epithelium also. When, by reason of altered blood-pressure, the glomeruli cease their activity the tubular epithelium has been proved to take up their function, so that excretion goes on. Nor is this assistance confined to temporary embarrassments of the glomeruli. When by reason of disease many glomeruli are destroyed, as in advanced interstitial nephritis, the output of urinary water is often largely increased. This may be due to hypertrophy of the remaining glomeruli but the widening of tubules and the endothelial type of their regenerated

<sup>1</sup> The infiltration theory was enunciated by Ludwig, and was supported with modifications by Hans Meyer and Koranyi, while the secretory theory was upheld by Bowman, Heidenhain, and, again, with modifications, by Bartels.

epithelium suggest that they have assumed the work of excreting water at the expense, it may be, of their original function. This illustrates compensation exerted by one part of an organ in favor of another.

There is good reason to suppose that the action of the epithelium is not always supplementary to that of the glomeruli, but may be antagonistic or at least exerted in a contrary direction: the tubular epithelium can absorb fluid from the stream passing down from the glomerulus. Its absorptive and secretory power can be exerted either from body fluid to urine or from urine to body fluid. Ludwig erroneously supposed that the tubule was given its vast length to act as a corrective upon the lavish glomerulus, which, like a filter, passed out urinary constituents in the same degree of concentration as that in which they existed in the blood, subsequent alterations being a function of the tubule. This much we may retain of his hypothesis, that the absorptive power of the tubular epithelium may be exerted in more than one direction.

What function is to be credited to the glomerulus, then, if it be not a filter? There is much reason in Brodie's contention that its peculiar structure allows it to act as a "propulsor," driving the water out of the capsule by its quick expansion; this function is necessarily apart from its vital secreting action. Let us digress, at this point, to indicate some of the characters that the epithelium of the tuft and the epithelium of the tubules respectively possess. It has been shown that the somewhat flat epithelium of the tuft lies on the capillary directly, without the interposition of any lymph space. By its great superficial area it approximates to the endothelial cell of the capillary, and thus, in the glomerulus, where mechanical forces (*e. g.*, blood-pressure) are prominent, the urinary water has to pass through only two flat cells, the capillary wall on the inside, and the outer flattened epithelial cell, which latter, by its shape and absolute juxtaposition, can allow the fluid to pass as readily as the capillary cell. But, on the other hand, it preserves enough of its epithelial quality to remember its function. It is a kind of frontier customs officer; it possesses complete power of allowing substances to pass, but, in addition, it possesses the power of selecting and turning back the undesirable elements. This is the specific power in which it surpasses its humbler endothelial brother. The tubule cell, on the other hand, works in an entirely different way. Between it and its capillary is a minute lymph space, and the lymph bathes it on one side and the urinary water in the lumen on the other. Here the layer of lymph exists to allow the cell to work, not in response to mechanical but to osmotic forces. The blood and the lymph make their exchanges, and the lymph and the cell make theirs; the lymph thus becomes a kind of middleman, and while breaking the continuity of mechanical forces, substitutes the medium by which osmosis can proceed. This being the case, it is readily understood that the osmotic process can go on as well from the urinary water to the lymph, by way of the cell, as from the lymph to the urinary water.

**The Excretion of Water.**—The most easily understood function of the kidney is the excretion of urinary water, mostly a glomerular but partly a tubular function; this varies in amount directly with the rapidity of

flow through the renal vessels, which rapidity may or may not be influenced by a rise or fall in blood-pressure; a certain minimal blood-pressure is necessary, but, if this be obtained, the effect of transient rises or falls in pressure is less apparent than the results obtained from an increased or decreased rapidity of flow.

Thus cardiovascular influences in general have their effect upon the excretion of urinary water, but the vasomotor influences exerted upon the kidney vessels themselves must be infinitely greater. Where these vasomotor stimuli arise and how they are conducted we do not know. Yet the results depending upon them are at times remarkable. What is the mechanism of hysterical polyuria, and why may a cannula inserted in the ureter cause anuria? Why does moderate venous interference lessen instead of increase the amount of water? Again, what is to be made of the immense increase of urinary water which may be found to follow the excision of large fractions of the kidney substance? Upon the answers to these questions we can only speculate, but, at least, they indicate how great is the elasticity of function in the matter of water excretion. While attention is directed to the importance of vasomotility, it must in addition be kept in mind that there is a cellular selective power in the epithelium and endothelium of the glomerular capillary, although we do not know whether the urinary water escapes through or between the cells or by both routes; whatever be the fact, the endothelium does possess a varying power of allowing fluid to pass, either by a shrinking of the cellular bulk and a consequent increase of the intercellular spaces, or by a distension of the vessel producing a flattening or thinning of the cells. It may be stated, however, as a probability that the excretion of urinary water is accomplished by a combination of several forces, acting together or separately, namely, the pressure and rapidity of the blood-stream, the personal power of the capsular epithelium and the endothelial cells of the capillary, and obscure influences on either or both of these brought about by nervous stimuli; all of these, again, being to a large extent under the dominance of local vasomotor nerves. The influences which act upon the output of urinary water are thus very far reaching, and are such as will react to many physiological, to say nothing of morbid changes; the difficulty of telling how far the kidney itself is at fault, or how far it is merely proving an adjuvant to some other system, is apparent. The kidney may act the last-named good part for the sake of some other organ, such as the heart, and it may do this so long and so continuously that it becomes a slave, and bears the brand of its master in a physical change which is indelible.

**The Excretion of Solids.**—The separation of the solid substances of the urine forms the next function of the kidney, and these substances fall at once into two groups, inherently useful materials (which are in excess, such as sugar in alimentary glycosuria, or which have served their purpose, such as pigments), and substances that are inherently harmful. The latter class embraces many end products of metabolism which we are accustomed to consider as the normal constituents of urine, as well as incidental substances introduced from without and substances produced by pathogenic agents in the body. As has been



indicated above, the power of excreting solids seems to be shared by the glomeruli with the tubular epithelium; in the glomeruli there is no doubt a certain degree of extrusion by mechanical force of substances in crystalloid or soluble form in the blood which are permitted by the glomerular epithelium to pass. It seems wrong to deny to the glomerular endothelium a certain ability of selection, because we admit it for capillary walls elsewhere in the body, and, if there be no selective power in the endothelium, that of the epithelium must be exerted through the barrier of the capillary wall. Some substances no doubt escape through the intercellular spaces in the capillary wall and the glomerular epithelium, spaces which although of size varying with the degree of distension, are never large: it seems probable that colloid molecules like albumins are always too large to escape through these, while perfectly soluble substances like sugar can do so in minute quantity. If inflammation or other destructive process has been at work, the way may be clear for molecules of any size. The epithelium appears to be able to take up colloidal substances from the blood. The process here must be very complex—a combination of mechanical filtration, endothelial selection, more refined epithelial selection, and perhaps osmotic exchange as well. In the tubules, on the other hand (bearing in mind what has been said previously as to the insulation of the tubular cell by an infinitesimal layer of lymph), the process is reduced to a combination of selection and osmosis. Perhaps, after all, selection is but an expression of osmotic force. If we have any force other than osmosis, we must admit that it is exerted this time across the barrier of the lymph space and the basement membrane. Further, the renal epithelium has the power of synthesis, and forms complex substances that are not apparent as such in the blood or lymph, such as hippuric from benzoic acid, as well as the power of analysis, breaking down other substances, as creatin to form creatinin. These changes are due to the formation in the tubular cell of an enzyme which has been called *histozyme*, and it is a significant fact that it has an interchangeable action, changing benzoic acid and glycol to hippuric acid, and the contrary. The bearing of this quality upon the supposition that the renal epithelium is free to exert its power toward absorption as well as toward excretion is obvious.

Lastly, has the kidney an internal secretion in the sense in which we speak of the secretion of the thyroid, the pituitary, or the adrenal? One is tempted to think so, although it must be admitted that we have no evidence that is undeniably certain; unfortunately, extirpation of the kidneys is followed by death from symptoms which are explicable on other grounds than the absence of a specific secretion; but in nephrectomized animals death can be postponed for a short time, but not averted, by the administration of the juice of the fresh organ. The administration of raw kidneys in case of renal insufficiency has not yet been so successful as to enable us to deduce that a specific internal secretion exists.

In considering normal urinary excretion, it seems necessary, above all other things, to acknowledge the vast importance of the dependence of one part of the kidney mechanism on another, and the readiness with which one part takes up the work of another, remembering, at the same

time, that there is a high degree of individuality in the renal cells themselves, so that the degree of functional activity or of implication by disease may vary greatly in different parts of the same organ.

### THE PATHOLOGICAL PHYSIOLOGY OF THE KIDNEY

**The Relation between the Blood and Kidney Excretion.**—While the kidney has a specific power of secretion or excretion which may be reserved for special occasions, or, on the other hand, which may be doing subsidiary work all the time, there is yet a very important, quasi-mechanical excretion going on constantly by the glomeruli. This was naturally one of the earliest facts to be observed. The glomerulus, a mere coil of capillary, was seen to have a large afferent and a small efferent vessel; the blood-pressure at the source of the renal artery is high, that at the mouth of the renal vein low; it was thought that the excretion of urine was the expression of the difference of force between these, plus the amount that was excreted in the secondary system by which the tubule is supplied. It will be remembered that the arteriæ interlobulares carry most of the blood entering the kidney directly to the glomeruli (although some of it goes to the vessels in the intertubular spaces), and that the efferent glomerular vessels are distributed to the intertubular tissue to supply the tubules after the blood has gone through the glomerulus. The kidney thus resembles a compound engine, in that most of, if not all, the blood goes to the high-pressure glomerulus, as the steam goes to the high-pressure cylinder, thence much of it goes to the low-pressure tubular capillaries, just as the steam, deprived of much of its expansive force, goes to the low-pressure cylinder; in all this the mechanical advantage is evident.

The result is that, ordinarily, the blood-stream is inflicting a certain wear and tear on the glomerulus; the wear and tear depends upon the amount of work that is being extorted from the mechanism, or, expressed differently, depends upon the persistence with which blood at high pressure is supplied to the glomeruli; the compound engine after a hard run is allowed rest, but the glomeruli have no such relief; in any middle-aged kidney, or a kidney that has experienced hard, continuous strain, there are the so-called hyaline glomeruli which have still the form but none of the functions of glomeruli; as the body has no means of supplying new glomeruli, the blood force is no longer expended on the high-pressure glomeruli, but falls direct, to a great extent, upon the low-pressure secondary circulation, which was never built for such high-pressure work; it is likely, then, that degeneration goes on here all the more quickly, and stress undoubtedly leads to a rapid fibrosis; it is not difficult to imagine that a degenerated glomerulus leads soon to a damaged or quite inefficient tubule, not only from the results of this stress but because the inefficiency of the glomerulus brings it about that the tubular cells are no longer thoroughly washed by the free flow of urinary water.

Another factor, which seems no less important, is the *quality of blood* that is supplied to the entire capillary system. The blood brings deleterious

substances which injure structures in their passage, and the structures also have to take their nutrition from this source; the more deleterious substances there are the worse is the cell food, and, therefore, the poorer the work done by the cell; the cumulative nature of such a bad state of affairs is easily apparent. Thus it is brought to pass that perfection of selective power is lost, and substances that were once held back are allowed to pass through, and, on the other hand, substances whose appearance in the urine was dependent on kidney efficiency no longer appear there. In such circumstances water is excreted by skin and bowel; salts, such as chlorides, may escape by the intestine; nitrogen may, to a great extent, escape by the same way or even by the saliva in small amounts, and the well-being of the organism no longer depends on the kidney but on the excellence of the adjuvant systems.

**Tubular Functions and Disturbances.—The Functions of the Tubule and its Behavior when Irritated.**—To the tubular epithelium we are in the habit of ascribing certain functions connected with the partial excretion of salts and other solids, as well as the synthesis of uric acid and the analysis of creatin and other bodies; but these are doubtless but a small part of the work of so complex a structure, and our knowledge of the actual secretory power of the tubular cells is gathered from sadly uncertain modes of investigation; the convoluted tubule and the ascending loops of Henle excrete uric acid; but what is to be said for the tubular areas that as yet, like brain areas, are “silent?” What mean the modifications of epithelium in the various parts of the tubule? We can scarcely guess. One is tempted to indulge in the fancy that the tubule may some day be divided off as to function, in the same way as the alimentary tract is; that, just as there is a specialized process in each part of the latter, there may be in the former; also, that the processes of absorption and reabsorption that go on repeatedly as the intestinal contents pass down may, in some less degree, be repeated in the tubule.

The convoluted parts of the tubules are those in which we mark most constantly the changes wrought by toxins; in fact, the strictly medullary parts of the tubules are as yet of but little use to us, so far as the microscopic determination of pathological change is concerned. Analogy leads us to suppose that if these last were concerned only in conduction we would have a less specialized lining for them.

Experiments with pigments in the hands of Heidenhain, Adams, and many others, have proved useful in the determination of functions of different parts of the tubule; various pigments are put into the animal body, and when the animal is killed, after a shorter or longer period, the position of the pigment granules in the kidney cell is determined. The conclusions drawn therefrom are open to the objection that the position of pigment in the cell is not necessarily an indication of its route, but, if sufficient of such experiments be carried out, it is safe to assume that the distance (in the cell from the lining membrane) that the pigment has progressed in animals killed at various times after injection indicates whether the pigment is taken up from the blood or from the urine. It must be admitted, of course, that experimental animals are not exactly normal, and the very “give and take” of one part of the tubule and



another may perchance lead substances to be excreted in a way differing from that in the normal kidney.

The tubular cell is prompt to suffer from the effect of even transitory toxicity of the blood and lymph. With reference to the lymph, indeed, we will do well to remember that the lymph which bathes the cells intercellularly probably acts precisely as does the blood with reference to excretion, save that, there being no high pressure in its current, it exchanges its constituents with the urine and the cell juice merely by osmotic variations of the fluids. To toxic lymph and blood the cell quickly reacts, entering the state of cloudy swelling; this is the peculiar "ground-glass" appearance that the individual cell takes when it is damaged, and the kidney of almost every infective or toxic case shows it so distinctly that it may be determined by the naked eye. It probably is often undergone by cells in the course of life, and from it the cell can recover entirely. Careful study of the cell with cloudy swelling indicates that there is a disturbance of the osmotic relations, by which the bulk of the cell becomes much greater; the Altmann granules, instead of being arranged in definite rows, appear to be dislocated from this arrangement and are seen in apparent disorder. The cell in this state is undoubtedly less efficient, and, as was pointed out earlier in this chapter, there is at once a less perfect excretion by the cell, and its own katabolism is increased. So the vicious process continues until the individual cell has gone on to the stages of granular, fatty, or hyaline degeneration, as the case may be, all of which are supposedly more extreme than cloudy swelling; it may well be imagined that the results upon excretion are to lessen its efficient performance. Such a condition may become the beginning of a permanent insufficiency, and the kidney tubule may not be able to regain its state of perfect health.

When considering the damage wrought upon the kidney by toxins, it is essential, however, never to lose sight of the fact that there are two widely different classes of tissue involved, the parenchyma and the connective tissue. These differ widely in the extent of their reaction to irritation. The writer is in the habit of using a fanciful illustration for this: the parenchymatous cell represents the "professional man" in the community, specially trained, not to be replaced but by one of his own class, impressionable by even slight external stimuli, not prone to be physically hardy nor overgiven to reproduction. The supportive cell, on the other hand, is its "laboring-class" brother, not trained in any high, special task, whose supportive work can be replaced by any kind of tissue, even scar tissue, not readily impressionable, even by powerful, external stimuli, physically strong, and ready in reproduction. These two cells lie side by side in the kidney, exposed to the same toxic influences, but reacting to them each in its own way. A toxin strong enough seriously to damage the high-class cell is only strong enough to irritate the low-class cell to reproduction. When the high-class cell is killed by toxin, in the absence of regeneration by the remaining tubular cells, it leaves no one of its kind in its stead, and its place is occupied, but its function is not performed, by the progeny of its laboring-class brother. If some such plan be kept in mind, one is prepared to collate the effects

of toxin upon each kind of tissue, and so to form a right idea of the *total* result in the organ. When the condition of imperfect tubular excretion, referred to above, is prolonged, many cells die and are desquamated, and the toxins which sufficed to damage and even kill the cells are sufficiently potent to irritate the supportive structures to overgrowth; thus, hand in hand, the two processes go on until there is proliferated connective tissue where once was a tubule, and this is the process of fibrosis. The work of every destroyed tubule must be thrown on its surviving fellows, and if the kidney continue to perform its work apparently perfectly, it is done, nevertheless, at a price; the price is stress, which will have to be paid for by shortened life of the other tubules.

**The Effects of Toxins.**—What are the effective toxins? They are the toxins, so called, of the infective diseases, products of cell katabolism throughout the body, hemoglobin, many irritant exogenous poisons (of plant and animal origin), and perhaps many chemical products which we are accustomed to consider as the normal output of the kidney. This apparently brief narration includes a vast number of substances. The products of pathogenic bacteria are well known as having an irritant action on the kidney, but there are doubtless products of bacteria not known to be pathogenic which also irritate; the great numbers of bacteria in the alimentary canal are constantly producing substances with which the kidney has in part to reckon; and in constipation this responsibility is doubtless increased. Every cell that breaks down in the body has to be disposed of, and in cases of extensive damage, as burns, suppurations, and necroses, the kidney has to bear its large share of the excretion. With reference to exogenous substances, we have but to look at the belief that one food is better than another, that the red meats are harder on the kidneys than white meats, and a hundred other facts or fancies that make up our ideas upon diet; be they truths or errors, we have but to observe these to see that practitioners of medicine at least have given a large place to the responsibility of the end products of ingesta with regard to the kidneys.

**The Effects of Age.**—The changes produced by age may be considered physiological, and doubtless are, but physiological in the sense of being processes which are always occurring, which cannot be obviated, however hurtful. Every "old" kidney shows certain changes which appear to be of the nature of replacement fibrosis such as we have previously described; they appear to coexist with changes in the arteries, and in the very old make up a well-defined entity. What, then, are the causative factors here? If we knew the cause of arteriosclerosis the question would probably be answered: work, katabolism, stress, the hundred slight disturbances of all the tissues (whose katabolic effects must be disposed of) the fact that nothing lasts forever, the sudden jars, metabolic and chemical, of a blood-supply no longer perfectly cushioned by elastic arteries—these, and as many more, perhaps, go to make up the factors which cause the changes of age. The constant breaking down of cells is a strain on the kidney, the greater by so much as the kidney is older; but it must be said, on the contrary side, that the very fact that the

body is smaller and the cells fewer is of advantage to the kidney, because the output of such cells is less than in the body of full manhood; there is thus a kindly compensation in old age which tends relatively to lighten the renal labors.

Nevertheless, it often appears that the "old" kidney is a very efficient one; and this compensation is a virtue not to be ascribed more to the kidney than to the circulation. As the arteries become old and inelastic, the heart can no longer depend upon them for the necessary contractions which tend to raise blood-pressure in localized areas, and must perforce work harder and adopt a higher general standard of minimum blood-pressure, which is accomplished by hypertrophy of the heart. From the time at which this raising of the minimum blood-pressure commences, the tissues, even when most at rest, are yet exposed to a strain greater than that to which they have been accustomed; with the increasing inelasticity the minimal blood-pressure continues to rise. The kidney shares to the full degree in bearing this strain, and the constant stimulation—mechanical if no other—leads to productive processes in the supportive structures.

**Parenchymatous Change in General.—Albuminuria and Casts.**—As the kidney tubule is the unit of the kidney, and, so far as we can see, every tubule is built exactly like every other one, the parenchymatous derangements of the kidney can be narrowed down to the sum of the derangements of the single tubule, derangements that vary from cloudy swelling to complete disappearance and replacement. Slight changes often pass unnoticed, so far as any urinary sign is concerned, and, on the other hand, there are slight urinary changes, such as transitory albuminuria, with which we have not yet learned to coördinate the corresponding alteration in the kidney. Without entering into the question of albuminuria, it may be said that these transitory albuminurias must have a meaning; albumin has its place, and its place is not in the urine, so that "physiological," as a term applied to albuminuria, ought to mean not a normal process; but a process so little abnormal that experience has led us to know that its existence does not lead to more serious disturbance. Albuminuria can depend, too, upon causes which are not situated in the kidney itself; anything that prevents the exit of venous blood from the kidney may cause albuminuria; experimental temporary blocking of the renal artery may cause it, the upright position in some persons seems to cause it, or, to put it in another way, the recumbent position causes its cessation; also the distribution of increased pressure in pregnancy has been held to explain the existence of albuminuria. Under these circumstances, all or most of the albumin is excreted by the glomeruli. But in its occurrence, when there is disease of the kidney, the site of its output is uncertain, and may be tubular as well as glomerular.

Here it is in place, also, to make reference to *casts*. The blood-cast is an evidence of rupture of a capillary or other vessel in the glandular part of the kidney. The source of the epithelial cast is equally obvious, although it is formed sometimes of the original tubular lining and sometimes of epithelium that has been newly generated by the tubular cells; the histological nature of the cells concerned gives no accurate information



as to the site of its formation, and in all cases it must be remembered that the cast, when seen in the tubule, may be on its way out, and is not necessarily at the site of its formation; epithelial casts can be formed, too, by agglomeration of cells, so that the juxtaposition of its individual members does not always mean that they occupied that place in life, although it generally does so. Some hyaline casts are also of epithelial origin, although it is not possible to say whether the hyalinization occurred in life or after the cells were detached. Whenever they can be recognized as epithelial, casts mean that the kidney substance is, to this extent, destroyed. It is true that, normally, kidney cells are constantly paying their debt to nature by dying, and as such are being shed off, more or less altered. The appearance of single cells in the urine thus means nothing, but with aggregations of them it is different; if one may use a simile of a homely kind, the deaths of many men here and there in a community do no more than remind us of our mortality; but when a dozen members of one family circle die, we suspect a local cause. This is the state of affairs in the renal community when a cast appears; there is a local overturn of normal conditions where it originated. The statement has just been made that some hyaline casts are of epithelial origin; perhaps the majority are, but the subject has been the battleground of much controversy. It seems reasonable to suppose that hyaline casts can originate in three ways, from the epithelium itself, shed and altered; from coagulation of transuded plasma; and as an excretion of the tubular epithelium, or, better, as a separation of part of the tubular epithelium. These will be dealt with in their order.

Langerhans demonstrated the colloid alteration that epithelial cells undergo, by which they become glassy and transparent. Ribbert has long championed the second theory of formation. He considers that casts are formed of albuminous transudate hyalinized by the acid reaction of the kidney. His experiments certainly seem to bear out the contention, but Saundby concludes from their rarity in functional albuminuria that this is not a common source. Some hyaline casts give the reactions of fibrin and some do not. The supporters of the third theory contend that hyaline casts may be formed by the shedding of material which may be either the cell substance itself, that has imbibed water and has swollen up, or is an excreted product of the cell. The material referred to can be seen in tubules of a kidney which is the seat of moderate nephritis, and consists of globules or masses of varying size, which look like irregular droplets, which appear to be able to fuse together, but which at times appear to be only the spaces between the meshes of the detritus that is seen in the lumina. Ribbert contends that these are normal. Where such are present, the epithelium is often found low and, as it were, lopped off; when the epithelium is not truncated, it may be that the material has descended from a higher part of the tubule. It will be at once evident that a growing vital part of the cell is yet left, and this may be the reason why a kidney can produce vast numbers of such casts through a series of years, without suffering greatly in the process. Oertel and Rovida long ago referred to these "plasma rings," and discussed their probable relationship to hyaline casts. Bartels considered that

the hyaline cast is generally formed from an excretion of the cells, while admitting the possibility of its formation from the coagulation of albumin. Councilman, who has carefully studied the kidney, will not venture an opinion upon the nature of these structures, but, on the other hand, admits the likelihood that fibrin can form casts. There is good reason to suppose that hyaline casts arise in all three ways, as Saundby stated some years ago. All of them indicate a pathological state of the secreting structures, and a hyaline cast, therefore, viewed in its most innocent light, is an indicator of disease. Even when the cells are shed in numbers as casts, it is well to recall that kidney epithelium can be regenerated to a moderate extent over denuded areas.

**Changes in the Glomeruli.**—The changes which are found in the glomerulus in different forms of disease are manifold, but it is hard to refrain from grouping them into those which signify acute disease and those which signify chronic change, although the boundary between the two is difficult to place.

**The Capsular Space.**—Exudation of albuminous fluid and subsequent fibrin formation can occur, and this may either be absorbed, swept away, or may remain and become organized, so that partial or complete adhesion between the walls of the capsular space may occur, and, further, the glomerulus itself may become secondarily vascularized by new-formed vessels which run from the peripheral wall. Hemorrhage may occur into the capsular space. The lining epithelium may be so damaged as to become swollen, granular, and may be desquamated in a moderately undamaged or in a necrotic state, or in cases of less extensive damage it may actively proliferate. Degenerated cells pushed up from the tubules may appear in the capsular space, as was shown by Welch in the kidneys of cantharidin poisoning. In all this one may see, as has been suggested, the parallel that exists between the capsular cavity and the serous cavities, such as the pleura or the peritoneum (Cornil). It is not mere coincidence, but shows that the reaction to inflammatory, regressive, and progressive changes is everywhere in obedience to law.

**The Capillaries of the Glomerulus.**—In the capillary branches may be found bacterial, fibrinous, or hyaline thrombi; leukocytes emigrating through the walls have been seen by Councilman, although the occurrence of this phenomenon had for long been denied; cells, evidently the proliferated endothelium, are seen, sometimes yet adherent, at other times desquamated and degenerated. An increase of the cells between the capillaries is at times to be seen, which cells may prove to be mainly leukocytes; this is, naturally, the result of the emigration spoken of above, and this infiltration may not be found elsewhere in the kidney, indicating clearly the existence of irritants whose "first choice" is the glomerulus. The entire glomerulus rarely may be converted into a granular, necrotic mass, in which no individual features can be distinguished. Amyloid change of the capillary is familiarly known, and most common of all is the hyaline change which affects the vascular wall. Whether it occurs on its outer surface or its inner surface is uncertain, but the change begins in the distal parts of the loops and progresses until the lumen is partly or wholly occluded, and the entire tuft is

replaced by a hyaline mass, with an occasional narrowed blood-space in which the scattered nuclei of its lining cells still may be distinguished. Finally, the intercapillary connective tissue may be proliferated and the new-formed tissue ultimately shrink, pulling in the surface of the tuft by its contracting bands, just as happens in a "hepar lobatum;" this constitutes the lobulation that is at times so characteristic a mark of the damaged glomerulus.

The effect of the above-mentioned chronic changes on the size and appearance of the glomerulus can be well imagined. Side by side with small, hyaline, useless glomeruli will be found others of great size, which by compensatory hypertrophy are capable of doing their own work and more; the excess of urine in cases of interstitial nephritis is probably partly due to the high efficiency of these hypertrophied glomeruli, at least so far as the excretion of water is concerned.

**Changes in the Tubule.**—The alterations produced in the tubule are more simple than those in the glomerulus; we have here to consider only the changes that the individual cell may undergo. These are the various degenerations, cloudy, granular, hyaline, fatty, and "dropsical" (vesicular, vacuolar); as a result of degeneration the cell may be desquamated individually, or with others as a cast; it may be thrown off and become cemented to others while in the tubule, again forming a cast; or it may become necrotic and disappear as quickly scattered debris. It may present variations of size and of shape, which variations in turn affect the capacity of the lumen of the tubule. Into the tubule may be thrown blood or the precursors of fibrin, with subsequent formation thereof. All degrees of variation of the size of the lumen are found from the narrow lumen of cloudy swelling to the cyst. All changes in the epithelial cell are but temporary, and must be considered as acute, in the sense that a cell will not live long in a damaged condition. When the cell dies, its neighbors may be able to generate a new cell to take its place, which, in its turn, may undergo similar changes; if no such substitute is formed, the tubule, as such, ceases to exist, or remains only as a space in the connective tissue; if its glomerulus also be destroyed, even the space ceases to exist, and solid fibrous tissue finally replaces it.

The deleterious agents which affect the tubular epithelium may be in the blood or in the urine, and in either case the chances are that the glomerulus will have been first exposed to their action.

**Changes in the Interstitial Tissue.**—Space need not be occupied in describing the changes that the connective-tissue stroma undergoes, for these are the same as are undergone elsewhere by supportive tissues. It may be the seat of a migration of leukocytes, of an active or a passive œdema, of a liquefying or a coagulation necrosis, or of any one of the many degrees of proliferation of its own elements with subsequent fibrosis. These changes do not always march shoulder to shoulder with changes in the connective tissue of the glomerulus, because the latter have peculiar opportunities for exposure to irritants. The capsule of the kidney is practically one with the stroma of the organ, and need not be separately considered. Variations in the size of the organ are assisted not only by the changes in the total mass of the interstitial tissue but



also by variations in the size of individual tubules and glomeruli, to say nothing of the variation in bulk of the blood and lymph vessels and their contents.

### NEPHRITIS

Let us be thoroughly theoretical for a moment, and say that a nomenclature of nephritis cannot be perfect until we describe every kidney in terms of the changes that exist in (1) the glomerulus, (2) the tubule, and (3) the interstitial tissue. Even now we are assuming that the tubule is a unit, whereas a fuller knowledge of its different parts may prove it to be divisible. The accurate description of a particular kidney ought to be denoted as follows: glomerulus, change of  $x$  degree, tubule, change of  $y$  degree, interstitial tissue, change of  $z$  degree; another kidney would show glomerulus, change of  $r$  degree, tubule, change of  $s$  degree, interstitial tissue, change of  $t$  degree. We have indicated a dozen variations, temporary or permanent, in the glomerulus, any one of which may be accompanied by one or more of the variations to which the tubule is liable; combinations thus made by mathematical process are, to say the least, numerous; when we go farther, and find that every such combination may be again combined with any one of the variations in the interstitial tissue, the possibilities are legion. Such a nomenclature, alas, is quite impracticable; yet every classification of nephritic conditions which has been promulgated is an attempt to sort out this almost infinite series, and the classification that disposes of most is the best, but is equally certain to be the largest and most unwieldy. Most of us are content to use a working method of classification and nomenclature by which we name the lesion by the feature which happens to predominate. Yet two kidneys may present the same predominant feature, while the other characters may differ widely, and even the same predominant feature may have been attained by widely different processes. Having pointed out the inexactness of the "nomenclature of the predominant feature," we are inconsistent enough to fall back upon it.

It is with an apology that one ventures upon the oft-trodden ground of Bright's disease, especially because the subject will be dealt with elsewhere. Bright's disease comprises acute and chronic parenchymatous nephritis, chronic interstitial nephritis, and that form of acute interstitial nephritis characterized by an infiltration of fibroblasts, but not by leukocytes (scarlatinal nephritis), all of which are toxic, not infective nephritides; that is, the bacteria are not pathogenically present in the kidney itself, as occurs in calculous, tuberculous, or other true infective acute nephritides. It is timely here to point out that those who make distinctions between chronic parenchymatous and chronic interstitial nephritis do so with the understanding that neither one ever exists alone; interstitial change never exists without an accompanying parenchymatous change, undoubtedly brought about in successive generations of tubular cells by the same agent, and parenchymatous change cannot exist long without interstitial alteration following or accompanying it. Acute parenchymatous nephritis may be produced in a very short time,

a matter of hours, perhaps minutes, and obviously cannot be accompanied by an instantly produced fibrosis, for the nature of the latter process is that it can only be slowly produced. An observable acute parenchymatous nephritis can, however, occur in any kidney, fibrosed though it be, provided enough tubules be left to enable us to see the change. We may go even farther than this, and say that the process we call chronic interstitial nephritis, strictly speaking, is no more than a series of slight consecutive acute attacks, each of which leaves a few more fibroblasts behind, and that in the intervals, although the results of previous acute attacks remain, the disease is at an absolute standstill. The "ups and downs" of a nephritic are familiar to us; the exacerbations referred to constitute the "downs."

There are many terms constantly used to indicate the various types of kidney found in nephritics, and one hears of small white kidneys, large red kidneys, small red kidneys, large white kidneys, and yellow kidneys, until one may be forgiven if he becomes confused; we do well to remember the extreme uncertainty of predicting the kind of kidney from the clinical symptoms and signs, and the habit of referring certain clinical signs to a "large white kidney" or some other such kind is to be discouraged. It may appear from the foregoing that an attempt is made to array all inflammatory and quasi-inflammatory changes in the kidney under three or four headings, modelled upon the terminology of Bright. Such is not the intention. It is well known that there are diseased kidneys which do not conform to such types: some toxins affect largely or entirely the glomeruli; others cause a change that is almost entirely confined to a particular vascular area, such as that connected with the capsule: active and passive hyperemias lead to well defined changes that are not proved to be inflammatory, but which on the other hand are not purely nutritional. A large and important class is that of arteriosclerotic kidneys, which approximate to those of interstitial nephritis, yet with important differences. Obviously these various states cannot be classified under any such simple headings as those referred to. In the absence of a perfect classification, and in the absence of expectation of ever attaining a complete yet simple classification, it may yet be pointed out that a division into acute parenchymatous, chronic parenchymatous, chronic interstitial and infective nephritides will embrace most of the lesions that are encountered, and will constitute a working basis for all but the experienced pathologist, who may safely be left to his own devices.

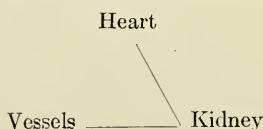
**The Varieties of Nephritic Kidney.**—We have indicated above that the two main forms of chronic kidney damage go hand in hand; there is in reality a wide range of lesions, at the extremes of which stand, at one end, the kidney whose most prominent lesion is parenchymatous; at the other end, the kidney whose most outstanding character is interstitial change. Between lies every possible degree of combination. When we find a kidney which combines the characters of both to such a degree that neither is conspicuous over the other, we make a compromise, and call it a mixed nephritis.

The changes that specially mark parenchymatous change are that

the kidney is big, plump, firm, yet resilient, often "hog-backed," and it has a wide cortex, often swollen. Those that indicate the kidney of the interstitial type are that it is small, hard, nodular, with a large fatty pelvis and a narrow irregular cortex. The former kidney is generally red, the latter pale, and these two are the types called "large red" and "small white." Further color modifications of these may exist according to the more or less accidental amount of blood in the organ at the time of death, although it would not be correct to say that the presence or absence of excess of blood is a fortuitous circumstance. Anemia of the body causes pallor of the kidneys as of other organs, and hyperemia, active or passive, will give a dark red color; fatty change in the epithelium may be so extreme as to give a yellowish or dirty white color to the cortical structures,<sup>1</sup> and a combination of this with hyperemia is one of the sources of the so-called "mottled" kidney.

Is there any relationship of these large and small kidneys one to the other? It has been known since the days of Bright that some large kidneys of the parenchymatous type progressed to become small ones of the interstitial variety. This is probably always so, provided the patient lives sufficiently long, but many succumb while the kidneys are yet large. There are, however, small granular kidneys that have never been larger than normal, that have, on the contrary, undergone a slow replacement fibrosis—the so-called primary renal cirrhosis or granular atrophy. The end result of this process does not markedly differ from the end result of interstitial nephritis, but it is presumably a process of quite different etiology.

These interstitial changes in the kidney are intimately connected in many cases with hypertrophy of the heart, especially of the left ventricle, and with arteriosclerosis. We find that many people die with certain lesions of these three systems in whom one cannot lay the blame on one system rather than on another. Does the hypertrophied heart lay so much stress upon the vessels and the kidney as to damage them, or does the vascular change precede the others, or is the renal lesion the primary one, or is some widespread toxin responsible for all three at the same time? Speculation upon these questions is as yet unending, and so much has been brought forward in support of a positive answer to each one that no firm basis yet exists on which to make a decision. For purposes of demonstration to students, the writer is in the habit of indicating the combination diagrammatically by an equilateral triangle; at one angle is *heart*, at another *vessels*, and at the third *kidney*, thus:



Then having pointed out the intimate physiological relationship existing among the three, one may rotate the triangle, and it matters

<sup>1</sup> Kidneys of this color may fail to give the chemical reactions of fat.



little which angle comes uppermost, as the three constitute a "triple alliance" which may fairly be said to represent an entity of disease.

Changes in the stroma of the kidney, however extensive, are not of themselves reflected in the urine, but the accompanying parenchymatous alterations are, and it is the glomerular and tubular defects which give the urine its pathological characters. But we have, by long observation, been able to see that the parenchymatous and interstitial changes go together in such definite proportions that we are able to prognosticate the latter from the former. In a general way, a granular kidney is associated oftenest with much urine of low specific gravity and little albumin, whereas the large parenchymatous kidney is often associated with a more moderate amount of urine, with much greater albumin loss and more frequent casts. As for frequency of casts, we have to remember that their numbers must never be considered apart from the amount of urine, and that the degree of disease being equal, the kidney with most tubules will shed most casts.

The uncertainty of prediction of the extent of disease from the observation of the kind and number of the casts is very great. Max Brödel, of the Johns Hopkins Hospital, has compiled some interesting figures as to the number of tubules and glomeruli in the normal kidney. He has estimated that there are approximately 4,000,000 tubules and glomeruli in the two kidneys, aggregating about 75 miles in length. Based upon this calculation a tubule secretes between two and three drams of urine in a lifetime of seventy years. When we consider that a urinary examination takes cognizance of the production of casts or the shedding of epithelium from but an infinitesimally small part of this area, and that all forms of change resolve themselves into three or four different kinds of casts, it seems reasonable to make mental reservations with any stated diagnosis which is based upon the number and the kind of casts present.

**The Functional Competence of the Kidneys.**—Many an individual is at this moment the possessor of sadly damaged kidneys who yet enjoys relatively good health. Such a man has not the "margin of safety" possessed by a normal person, but nevertheless succeeds in weathering serious storms. Should the question of operation arise, the surgeon may be frightened by the amount of albumin or the number of casts to be found in the urine. It is obviously difficult from such observations to state how good or how bad the kidneys are. Is there any means by which a proper idea of the competence of the kidneys for their work can be obtained? Experimentally there are certain methods by which the functional capacity of the kidneys can be measured. Of these, the most serviceable is that known as the "phenolsulphonephthalein test" of Rowntree and Geraghty.<sup>1</sup>

Phenolsulphonephthalein when injected subcutaneously, intramuscularly or intravenously is excreted rapidly and practically quantitatively in the urine, in which it can be determined by the addition of

<sup>1</sup> *Jour. of Pharm. and Exper. Therap.*, 1910, i, 579; *Jour. Amer. Med. Assoc.*, 1911, p. 811; *Arch. Int. Med.*, 1912, ix, 284; *Trans. Cong. Amer. Phys. and Surg.*, 1913, ix, 23.

alkali and comparison with a standard phthalein solution. After intramuscular injection normally 50 to 65 per cent. is recovered in one and 60 to 80 per cent. in two hours. Half an hour before administering the test the patient is given 200 to 400 cc. of water to drink in order to insure a free urinary secretion. One cc. of phenolsulphonephthalein solution containing 6 mg. of the dye is injected intramuscularly, preferably into a lumbar muscle. At the end of one hour and ten minutes and of two hours and ten minutes the bladder is emptied, a catheter being used when obstruction or inability to empty the bladder is known to be present or is suspected.<sup>1</sup>

Each sample of urine is treated with sufficient 25 per cent. NaOH to elicit the maximum intensity of color and diluted with distilled water to one liter. The solutions are thoroughly mixed, small portions filtered off and compared in a calorimeter against a standard solution containing 6 mg. of the sulphonephthalein diluted to one liter with the addition of alkali. The calorimeters usually employed are Rowntree and Geraghty's modification of the Autenrieth Königsberger calorimeter and the Dubosq, but when neither of these is available fairly accurate determinations can be obtained by means of two graduated cylinders of equal caliber, equal quantities of the standard and of the diluted urine being placed in the separate cylinders and the standard diluted until the colors in the two cylinders become identical when viewed transversely.

The test is of great diagnostic and prognostic value in renal, cardio-renal, and cardiac diseases. In acute nephritis frequent repetitions of the test are necessary since marked renal functional changes occur with considerable rapidity. In mild chronic nephritis the excretion of the dye is but little reduced, while in severe nephritis it is markedly decreased or even suppressed. Marked diminution or suppression usually occurs in uremia, and impending uremia is frequently indicated, when routine clinical and urinary studies give no suggestion of it. Passive congestion only effects the phthalein output when of a severe grade and slight circulatory improvement is associated with prompt improvement in the phthalein excreted. The test is of great assistance in the interpretation of cardio-renal cases, since it can reveal the relative responsibility of the heart and kidney.

A marked decreased phthalein output always indicates severe functional involvement of the kidney, but a normal output does not mean a normal kidney, since in mild grades of chronic passive congestion and in some cases of chronic parenchymatous nephritis the phthalein output is not diminished. The test constitutes the most reliable individual test of renal function, other selected tests being used according to the nature of the case, *e. g.*, studies of sodium chloride or water excretion in oedema,

<sup>1</sup> Following intramuscular injection the dye in health appears in the urine within ten minutes, while in disease it is usually delayed. In order to accurately determine the time of appearance a catheter is passed into the bladder and the bladder emptied immediately following injection. The urine is then allowed to drop from the catheter into a test tube containing a drop of NaOH and the time of the first appearance of the pink color noted. The urine is subsequently collected for one hour and two hours.

of lactose excretion in mild congestion or nephritis, while for corroborative evidence when the phthalein output is low in severe nephritis, the presence of cumulative phenomena should be determined, low freezing-point, increase in blood-urea, and total non-protein nitrogen. In any renal disease repetition of the test reveals whether the pathological process is progressive, stationary, or retrogressive.

In patients with prostatic obstruction, a test of this kind guides the surgeon fairly accurately in selecting a time for operation when the kidneys are competent, better than the estimation of the urinary output, the total urinary solids, the urea, or the total nitrogen. It may be said, in general, that kidneys responding poorly to this test will probably behave badly subsequent to operation, if such be undertaken.

Tests of like purpose are made by the use of methylene blue, indigo-carmin, rosaniline, and phloridzin. Ambard has devised a formula which depends upon the relative amounts of nitrogen in the urine and in the blood, which is used as an indication of the competence of the kidneys. Literature dealing with all these methods has appeared in great volume during the last three years.

### THE KIDNEYS AND FOOD AND DRINK

The statement frequently made, "that more men die from overeating than from overdrinking," if true, refers no less to the kidneys than to the liver. Most articles of diet contain one or other of a long list of substances which are not easily excreted; they impose extra work upon the healthy kidney, and they are able to damage the unhealthy kidney. To restrict a healthy man's food because of a possible danger to his kidneys is not necessarily rational, even if it were possible; but we should adopt every means we can to spare the already diseased kidney, and the healthy kidney in times of stress, such as occur during the course of fever, of infections, and of intoxications. In these last the kidney may be so near the point of breaking down that injudicious diet may supply the necessary additional irritation to cause the breakdown.

We have a preconceived idea that bland substances with a high proportion of water are kindly toward the kidney, while substances or fluids that are highly diuretic are considered to entail increased work upon the organ, and many condiments are thought to be actually injurious. These views appear in the main to be correct. In one sense, water is the best diuretic, and it is possible to wash the tissues as it is possible to wash the face, the ingestion of increased water and the consequent increased output of urine advancing the metabolic overturn in the whole body. But circumstances alter cases. We must agree with von Noorden and his school when they declare that there are times when the kidneys refuse to be washed; these observers have held with much reason that a kidney totally insufficient, that is, the kidney of anuria, is as unable to excrete water as anything else. Von Noorden even goes so far as to hold that to such a kidney water is as irritant as urea. Whether this be accurate or not, the kidney as persistently refuses to excrete the one as the other; restriction of fluids is therefore rational enough in this,



that when the blood-pressure tends to be high and œdema is occurring, it is useless, or worse, to add to both. As soon, however, as the kidney begins to express its readiness by a resumption of its water excreting function, the time has come when it will submit to washing.

When kidney incompetence is evident, as in anuric or oliguric states, the withholding of food may be necessary; but in cases in which the physician is required to exercise supervision lest the kidney be damaged by an infective disease, when his work is really preventive rather than curative, what form of diet may he adopt? We must supply the body with food whose products are easily excreted, and we must avoid the use of drugs that are difficult of excretion. It is generally admitted that urea, creatin, hippuric acid, and phosphates are hard upon the kidneys. Urea is the result of ingestion of albuminous food; creatin exists largely in meat extracts and broths; meats and eggs are essentially protein, milk is moderately so, cream much less so than milk, starchy foods scarcely at all. Cereals, fresh vegetables, and boiled fruits are also innocent in this regard. Green vegetables, fruits containing kernels, and cranberries contain relatively large amounts of benzoic acid, which is synthetized to hippuric acid, which also is difficult of excretion; apples, pears, grapes and raspberries contain little of it. Phosphates are largely present in meats, eggs, and milk; but von Noorden and others declare that the use of calcium carbonate with milk causes the excretion of much of the phosphoric acid by way of the alimentary tract, so that in this way the work entailed by a milk diet can be largely reduced; uric acid and the alloxuric bases come especially from meat glands, such as thymus, liver, and kidneys, and are moderately toxic to the kidneys; meats of all kinds contain extractives, and the so-called dark meats to a greater extent than the light meats. Adler, in a review of the subject, concludes that the prevalent idea that the subject of renal disease ought to eat light rather than dark meats is correct, and that these meats boiled contain the harmful factors less than when roasted.

Condiments which are generally supposed to impose work upon the kidneys are pepper, curry, mustard, garlic, and nutmeg; and with reference to drugs, one does well to remember the effects of cantharides, copaiba, turpentine, salicylates, carbolic acid, resorcin, lead, copper, silver, mercury, and boric acid, and even iodoform and tar preparations.

Of all the articles of every-day diet, what is left to us to use that will not entail work upon the kidney? Judged by analysis, and supported by empirical knowledge, milk is a more suitable food than any other thing; but this is not meant to be a declaration in favor of "milk diet" as a routine treatment of renal insufficiency, because evil has been wrought by a slavish adherence to a milk diet, as if it were a rule.

These statements are not made with any view to declaring a treatment for renal incompetence, or of forestalling the articles dealing with the renal diseases, but merely as a kind of working basis that one may keep in mind as an assistance in determining a diet in any case of illness in which the kidneys are specially liable to attack (as in scarlet fever), or in any case in which a damaged kidney leads one to be cautious lest the disease be aggravated.

## CHAPTER XII

### MALFORMATIONS OF THE KIDNEY, CIRCULATORY DISTURBANCES OF THE KIDNEY

BY JOHN McCRAE, M.D. (TOR.), M.R.C.P. (LOND.)

#### MALFORMATIONS OF THE KIDNEY

THE malformations of the kidney are of very slight clinical importance, especially to the physician; most of them, in fact, are but curiosities which lie undiscovered unless disclosed at autopsy.

**Absence.**—Total absence of kidney tissue is generally combined with abnormalities of the sexual organs, and is not consistent with viability. There are in existence case reports professing the contrary, but they are not credible.

Absence of one kidney, however, is fairly common, the writer having seen eight cases at autopsy. It is said, however, that in many so-called cases of absence of the kidney careful examination of the connective tissues of the region reveals that kidney substance may exist. No such microscopic examination was made in the eight cases to which reference is made. Once it was associated with a bicornuate, and once with a unicornuate uterus, and in many cases some anomaly of the sexual organs exists in association with it. The adrenal generally exists independent of the absence of the kidney, and sometimes a blind ureter opens to the bladder. The importance of this last fact is that the cystoscopic finding of a ureteral orifice is not perfect evidence of the existence of a kidney. With the development of radiography, and its combination with the use of the cystoscope, the clinical diagnosis of anomalies of kidney and ureter has become possible, and the recognition of such anomalies may assist the surgeon greatly.<sup>1</sup> The blocking of a ureter by any cause becomes much more serious in a case of unilateral kidney than in a normal case, but this has a surgical rather than a medical bearing. Cases of unilateral kidney are generally provided with a normal or almost normal amount of kidney tissue, thanks to the hypertrophy or hyperplasia of the existing organ. The chief practical point in connection with unilateral absence of the kidney is that it gives a rational basis for the surgical rule that before a nephrectomy is performed the presence of the other kidney must be demonstrated. The writer was present on one occasion in which the surgeon's care in this respect prevented him from removing the only kidney.

Failure of full renal development may be associated with a state

<sup>1</sup> Braasch, *Ann. of Surg.*, 1912, lvi, 726.

called "renal infantilism,"<sup>1</sup> occurring in ill-developed children and manifesting itself by polydipsia and polyuria.

**Anomalies of Shape and Position.**—Persistence of the fetal lobulation of the kidney is at times observed but has no clinical importance, nor have those departures from the conventional shape of the organ which are often seen. Sometimes the kidney assumes a shape which bears no resemblance to the normal organ, but this is not generally associated with any reduction in quantity of the kidney tissue, and makes not the slightest difference to the possessor. Fusion of the kidneys is chiefly of anatomical interest, the most familiar form being the well-known horseshoe kidney, in which the lower poles of the two organs are joined by a bridge of kidney tissue. Disease arising in such a kidney may be difficult of recognition; it is stated that the mere existence of the anomaly may lead to abdominal pain centrally situated, relieved by the recumbent position.<sup>2</sup>

**Anomalies of the Renal Arteries.**—The renal arteries may show varying irregularity in size, number, and position. In 1200 kidneys examined, 21 per cent. showed variation from the normal, a fact which is of interest to the surgeon, since the ligation of an aberrant branch may be overlooked.<sup>3</sup>

**Displacements.**—The kidney may be fixed in almost any abnormal position on the posterior wall of the abdominal cavity, most frequently at the edge of the pelvis; an organ so situated may be at times palpated, and may cause confusion in diagnosis, but no rule can be laid down for the avoidance of a mistake.

**Mobility.**—Gradations of mobility exist, from the kidney which is all but fixed to that which can be pushed into any corner of the abdominal cavity. The latter, although its dislocation is largely an acquired character, has probably a congenital laxity of fixation from the first. Anomalies of shape and site are not infrequently combined with undue mobility when the latter is of congenital origin.

**Congenital Cystic Kidney.**—The condition known as cystic kidney is at times congenital. Both kidneys, more rarely one, may be composed of a number of thin-walled sacs, of varying size, containing usually clear, yellowish fluid; these cavities are sometimes lined with epithelium-like cells and are closed. The walls are fibrous and may contain islands of renal parenchyma. Such kidneys may be found in the fetus, sometimes so large as to impede labor, or in the infant, or, finally, in the adult past middle age. While these are found at an age past middle life, it by no means follows that they have developed in adult life; on the contrary it is generally conceded that they have a congenital basis. The statement that they are rarely found before fifty years of age may be due to the fact that the rest of the kidney substance is adequate until the time of the discovery, and that the renal competence of earlier years is sufficient to tide over the possessor of a cystic kidney until that age. In the light of our knowledge of cysts resulting from nephritis, it is not easy to imagine

<sup>1</sup> Miller and Parsons, *Brit. Jour. of Children's Diseases*, 1912, ix, 103

<sup>2</sup> Rovsing, *Zeits. f. Urol.*, 1911, v, 585.

<sup>3</sup> Eisendrath and Strauss, *Jour. Amer. Med. Assoc.*, 1910, lv, 1375.



any other than a congenital beginning for those completely cystic kidneys that are observed in advanced life; it must be admitted that the sacs may have greatly increased in size as time progressed.

The generally accepted view of the causation of congenital cysts of the kidney is that failure occurs in the accurate junction of the masses of nephrogenic tissue (later called the renal vesicles, which ultimately form the tubules proper) with the outgrowths from the Wolffian duct which form the pelvis of the kidney.

A strange feature of this anomaly is that it has been found in several members of the same family, and mother and daughter have been observed similarly afflicted. It has been found, also, associated with cysts of the liver, and in a case from our own laboratory with cysts of the liver and pancreas. Professor Adami, discussing the latter case, thinks that the so-called cystic diathesis is rather a disposition to failure to overcome moderate obstruction of the ducts than a real liability to the formation of cysts. The cystic part of the kidney takes little or no part in urinary secretion, although it is conceivable that tubules might still remain in the walls of the cystic sacs; for all practical purposes the cystic part of the kidney has no influence for good or evil on the urine. Symptoms have been sometimes credited to a cystic kidney that really belonged to the other non-cystic organ.

The special features of the condition in adult life are: (*a*) Renal tumor, general bilateral, the location of which is usually readily recognized; (*b*) the occurrence of hematuria, which may be present at long intervals over a period of years; and (*c*) the usual urinary findings of chronic interstitial nephritis with the common changes in the vascular system, arteriosclerosis and cardiac hypertrophy. Osler has noted the occurrence of marked pigmentation of the skin in some cases. The termination is usually from uremia or cardiac failure, rarely from complications which follow the rupture of a cyst. The treatment is that of chronic nephritis, except in the rare cases in which the condition is unilateral, when removal of the affected kidney is possible.

### CIRCULATORY DISTURBANCES IN THE KIDNEY

**Anemia.**—Anemia or ischemia of the kidney may result as part of a general anemia, such as occurs in cancer, tuberculosis, or pernicious anemia, or may be caused by local agents of an organic kind which prevent ingress of blood to the kidney, or it may result from spasmodic contraction of the arterial wall. When there is a general anemia of all the tissues, the effect upon the kidney is that it undergoes a slow process of degeneration, produced by imperfect nutrition of the cells or imperfect removal of the waste products; this, however, is of little practical moment, as it is overshadowed by the effects of more important changes in other organs. The ultimate result may be an advanced stage of fatty degeneration of the parenchyma. Local anemia of the kidney may be produced by narrowing of the lumen from disease of the arterial wall, by thrombosis, or by the pressure of tumors or adhesions upon the artery; if severe

and long continued, the amount of the urine will be lessened, even to the extent of anuria; if the pressure be slight or temporary, its effects will scarcely be reflected in any urinary change. There are some cases of anuria, so-called hysterical, which are presumably due to anemia produced by spasm of the arteries, and, also arising in the nervous system, instances in which anuria results in one kidney from injury or irritation of the other kidney or of its ureter. We shall not endeavor to recite the anatomical appearances found as a result of anemia pure and simple, because we rarely see them except in experimental animals; nor the clinical signs, because there are none (save lessening of the quantity of urine) which can be safely asserted to be the result of ischemia alone.

**Hyperemia.**—The kidneys frequently become hyperemic, but the cases in which this happens are generally of such a kind that organs elsewhere in the body are more deeply concerned. Active hyperemia, such as occurs in inflammatory diseases, does not concern us here; passive hyperemia arises in two ways, either as part of a general venous stasis, or as the result of alterations of circulation which are local to the kidney.

Considering venous stasis in general, it may be pointed out that the venous outflow from the kidney will be lessened when the blood cannot pass freely to the heart because of direct obstruction, or when the current is slowed because the arterial force (primarily the heart) is weak. In conditions of cardiac incompetence both of these factors may be at work, and the question which one is more effective is not of consequence. When the heart is incompetent and the arterial flow weak, the result is cortical and especially glomerular congestion, with excretion of albumin into the capsules. This much follows experimentation; the results of local venous stasis are felt first, on the contrary, in the medulla. If the two work together, the entire kidney is engorged, there is excretion of albumin, and the epithelium of the tubules suffers by reason of imperfect oxygenation, imperfect nutrition, inability to get rid of its excretions by way of the blood, or a combination of these. The result is its degeneration. Such a kidney, seen macroscopically, is large, firm, and dark red; its capsule strips readily leaving a smooth surface, its stellate veins are injected, its cut surface may be œdematous or even bloody, is of a deep-red color, and its glomeruli are prominent. This is the condition generally described as "cyanotic induration." Many authors consider that, should this state be long continued, a slowly produced fibrosis is the result, which, although rarely great in degree, may yet suffice to produce contraction and consequent lessening of the size of the kidney. Oertel, however, in a recently studied series, does not find that venous stasis is followed by granular atrophy, and considers that such a change does not occur as the result of uncomplicated venous congestion, but from arteriosclerotic and other influences. Microscopically, the glomeruli are engorged and enlarged, and may lose their endothelium from pressure atrophy: the capsule of Bowman may be hyaline and stretched, and separation of fibres by œdema may be observed not only in the capsule but also in the intertubular connective tissue; the capillaries and lymphatics are dilated; the epithelium of the

tubules may show granular or fatty change, and some tendency to regeneration. In all this, the signs of inflammation are absent.

A passively congested kidney excretes a less amount of water than normal; the urine, therefore, is scanty, and for this reason of high specific gravity, highly colored, and readily precipitates its urates. Albumin is likely to be present in moderate quantity through the glomeruli, and casts in number commensurate with the destruction of epithelium; the latter being very gradual, casts are generally few. It is obvious that this condition is not easy to differentiate from an early nephritis; even the result of rest in a rapid clearing up of the signs and symptoms may not be sufficient to make the diagnosis plain; nevertheless, the recognition of the existence of a cause for the congestion may assist.

**Thrombosis of the Renal Vessels and Infarct of the Kidney.**—Thrombosis of the renal vessels, either artery or vein, or both, may occur. More than half a century ago it was recognized that the left renal vein of marantic infants was frequently the seat of thrombosis; the greater length of the left vein appeared to render it more prone to the process than the right. Thrombosis of the renal, as well as of other veins, was considered to be a sequence of a cachectic state, and today we can add little more to this than to point out the probability of its being the direct outcome of an infection that generally proves to be terminal. The appearance of a kidney with such a thrombosis, and the existence of symptoms or signs resulting therefrom, will depend largely upon the perfection of the collateral circulation; if the process does not prove fatal, the thrombosis will be found to have brought about a state of affairs not widely different from that found in passive hyperemia. Diminution of the urine, its high color, the presence in it of hemoglobin, and an icteroid tint of the skin are the external results that may be expected.

Thrombosis of the renal artery may occur from trauma, infection, or from disease of the wall of the vessel, but is rarely found. If the entire vessel be occluded, complete and rapid necrosis of the kidney results. Much more commonly, embolism of a branch of the renal artery, with its resultant thrombosis, is seen. Emboli may be infective or non-infective, according to the nature of the original process from whose site the embolus is derived. In the former case there is a metastatic abscess set up in the area concerned; in the latter, the well-known infarct is formed.

An infective embolus can and frequently does cause an infarct, but the rapid progression of the bacterial process causes the picture to be dominated by the features of abscess formation. When the embolus is non-infective, the case becomes one of infarction pure and simple. Such emboli are set free most often from thrombi or vegetations in the left side of the heart, but may happen when any foreign body, such as a mass of tumor cells, finds its way into the arterial circulation. Whatever be the appearance of such an infarct immediately after its formation (and this is still a subject of debate), when seen the lesion is a yellowish, sometimes golden, roughly triangular area, edged by a hyperemic zone of kidney substance; if superficial, it usually projects slightly from



the level of the kidney, and is as prominent on the external as on the cut surface of the organ. Sometimes the cortex is infarcted in its entirety, the medulla and the contiguous layer of cortex being spared, since the thrombosis has occurred in the interlobular arteries. All but the largest infarcts become replaced by fibrosis and ultimately are represented by depressed scars on the outside and fibrosed areas in the substance of the kidney.

Except in the case of the largest infarcts, there is usually no symptom or sign of their formation; a sudden pain in the kidney, with the appearance of blood or hemoglobin in the urine, in a patient prone to embolus, would justify the supposition that infarction had occurred; but usually, from the very fact that the primary disease is so serious, the existence of the renal infarct is unimportant; thus there is no need to deal with the question of prophylaxis or treatment, as these ends are served in the measures that are rationally adopted in the care of the primary disease.

## CHAPTER XIII

### ANOMALIES OF URINARY EXCRETION

By A. E. GARROD, M.D., F.R.C.P. (LOND.), F.R.S.

THE changes observed in the properties and composition of the urine in disease are almost infinite in their variety. Some are obvious to the most casual observer, gross deviations from the normal in tint, specific gravity, or volume. Others are readily detected by means of such simple tests as form part of the routine of clinical examination. Others, again, are only brought to light by elaborate chemical methods, or by the employment of instruments of delicacy and precision, for the use of which special training is required. Many have doubtless escaped detection up to the present time.

When the kidneys are the seat of disease the impairment of their functions may be manifested by imperfect excretion of urinary ingredients, of inorganic salts, or of the end products of protein metabolism. The urinary water may be greatly diminished in quantity, or may be much in excess of the normal amount. The impairment of function may also be revealed by diminished molecular concentration of the urine, while that of the blood is increased to a corresponding extent. Diseased kidneys may allow passage to the normal proteins of the blood, which it is one of their chief functions to retain in the circulation while allowing passage to waste products. Hence, albuminuria comes to be one of the most important of the signs of renal disorders. Lastly, products of the breakdown of renal structure, such as epithelial cells and tube casts, may bear witness to profound changes in the kidneys.

Such changes as the above, indicative of disease of the urinary organs, constitute only a small proportion of the deviations from the normal which are met with in disease. Anomalies due to metabolic derangements, in which the kidneys are in no way primarily concerned, are very numerous, and often quite as conspicuous. Hence the condition of the urine comes to reflect the state of the organism as a whole.

#### CHANGES IN THE URINE DUE TO DISEASES OF THE KIDNEYS AND URINARY TRACT

**Polyuria and Ischuria.**—Variations in the quantity of urine excreted are important signs in some varieties of renal disease. Diseases of the kidneys may give rise to polyuria on the one hand or to ischuria on the other. The ischuria, which may even amount to complete anuria, of acute nephritis may afford an even better indication of the degree

to which the excretory function of the kidneys is impaired than do the amounts of albumin and blood which the urine contains. The polyuria of granular kidney is a familiar sign; and of scarcely less significance is the development of polyuria, with abundance of albumin, in cases of parenchymatous nephritis which are entering upon a chronic stage.

Whereas, the destruction of one kidney or the blockage of its ureter does not profoundly or lastingly affect the volume of the urine, obstruction of the second ureter, or the simultaneous blockage of both, causes a form of anuria of great interest, on account of the nature of the symptoms which result, and of great clinical significance as urgently calling for surgical intervention. The intermittent passage of large quantities of urine, simultaneously with the disappearance of a renal tumor, is a valuable diagnostic sign in cases of unilateral hydronephrosis.

**Specific Gravity.**—Just as inferences based upon the volume of the urine are of little value unless the specific gravity is taken into account, the information which the specific gravity affords needs to be supplemented by a knowledge of the quantity excreted, in order that any satisfactory conclusions may be drawn from it. Moreover, seeing that the specific gravity varies widely at different periods of the day, it is important that the specimen tested should, if possible, be a sample from the day's total. The specific gravity affords a measure of the proportion of solids in solution, and deviations from the normal density of about 1.020 may result from excessive or deficient excretion of water or from variations in the output of dissolved substances.

Unless calculated for a normal volume of urine a low specific gravity does not imply a diminished output of solids in solution, for in association with polyuria there may be a daily output of excretory products which is in no way below the average, although, as in diabetes insipidus, the specific gravity may be very low. Even if the reading be low when corrected for a normal volume of 1500 cc. allowance must be made for the nature of the diet and the amount of protein which it contains.

However, in renal cases the indications which the urinometer affords are often of much value, as, for example, when, apart from any increase in the volume of urine, the specific gravity tends to fall; as it often does before the onset of uremic symptoms. In this connection it must not be forgotten that in the late stages of many maladies of chronic course but in which the kidneys are not directly implicated, when death is approaching urine of low specific gravity and scanty in amount is wont to be excreted.

**Cryoscopy.**—The method of cryoscopy, or determination of the freezing-point, recently applied to clinical purposes by A. von Koranji, owes its importance to the fact that the depression of the freezing-point of a solution supplies a measure of the osmotic pressure, and this again depends upon the number of molecules in solution. Thus, equimolecular solutions of two different substances will show a depression of the freezing-point of equal degree, and when two or more substances are in solution the depression will correspond to the total number of molecules, irrespective of their nature.

In dealing with an organic liquid such as blood or urine the conditions



are not so simple. Salts, such as sodium chloride, are dissociated into their component ions, and each ion, which counts as a molecule for the purpose in hand, has an equal effect upon the freezing-point with a heavy protein molecule. In the case of the urine the most abundant constituents, and especially sodium chloride, are largely responsible for the observed depression. Moreover, in the complex mixture, molecular rearrangements occur after excretion, and these, as Koppe has shown, tend to diminish the number of effective molecules. The conversion of urea into ammonium carbonate will have a like effect, and therefore it would be desirable to make the determination with freshly passed urine, whereas the results will have little value unless a sample of the excretion of twenty-four hours be taken. Again, the total number of molecules in a sample specimen will be largely determined by the bulk of the urine in the day, so that an unusually high freezing-point may depend upon a copious excretion of water as well as upon a diminution of the solid constituents in solution.

Accordingly, it is found that whereas the freezing-point of the blood of healthy persons deviates but little from  $-0.56^{\circ}$  C., that of their urine varies between  $-1.3^{\circ}$  and  $-2.2^{\circ}$  C. Chiefly on this account the indications afforded by cryoscopy of the urine alone, in cases of bilateral renal disease, are apt to be inconclusive as to the functional competency of the kidneys. When the freezing-point of the blood can be compared with that of the urine in such cases the results obtained have a much greater value. The accumulation of excretory products in the blood lowers its freezing-point, whereas their comparatively scanty presence in the urine has an opposite effect, and the two figures tend to approximate. In extreme cases the freezing-point of the blood may be equal to, or even lower than, that of the urine. In acute nephritis, recovery is accompanied by a progressive fall of the freezing-point of the urine to normal figures.

**Electrical Conductivity.**—The determination of the electrical conductivity of the urine affords another means of determining the number of contained ions. Here again sodium chloride plays the most important part in causing variations in the resistance offered. Molecules which are not dissociated do not favor conduction, and a urine of high specific gravity due to contained sugar may, nevertheless, have a high resisting power. Hence the indications afforded by electrical conductivity are different from those afforded by the freezing-point.

**Reaction of the Urine.**—This may afford valuable indications as to the condition of the urinary tract, but here again variations may equally result from conditions above the kidneys. Alkalinity due to the presence of ammonia and ammonium carbonate points to infection of the bladder or urinary passages, seeing that it is due to the decomposition of urea under the influence of bacteria. It is a prominent symptom of cystitis. It must be remembered, however, that certain microorganisms produce pyelitis or cystitis with acid urine.

Ammoniacal urine may be recognized by its peculiarly offensive smell and by the change to blue of moistened red litmus paper held above the surface of the liquid. Alkaline urine of this character deposits abundant crystals of ammonio-magnesium phosphate, and since it is

usually associated with cystitis, many leukocytes are, as a rule, present in the sediment, and the urine may swarm with bacteria.

**Albuminuria.**—One of the most important of the renal functions is that of refusing passage to the proteins of the blood while allowing a free passage to the end products of metabolism. This function appears to be a highly specialized one, for proteins foreign to the blood, unless present in very small quantities, are not at all held back to the same extent, as witness the free excretion of hemoglobin in the paroxysms of hemoglobinuria, and of the Bence-Jones protein by kidneys which are not the seat of disease.

With serum albumin, the blood globulin and fibrinogen the case is different, and although there are grounds for believing that minute quantities of these substances find their way even into normal urines, and that, occasionally, amounts appreciable by ordinary clinical tests pass through kidneys which are not seriously abnormal, in the conditions included under the name of functional albuminuria, the fact remains that the continuous excretion of appreciable quantities of albumin usually denotes renal disease, either primary or secondary to circulatory disturbances. Hence, albuminuria comes to be the most important of the urinary signs of disorders of the kidneys, and has a wholly different significance from the excretion of other protein substances in the urine.

Although it may be accepted as proved that the albumins of urine are actually blood-proteins which are not held back as they should be, the relative proportions of serum albumin and globulin are by no means those which prevail in the blood. Serum albumin usually preponderates greatly in the urine, but globulin is usually also present in varying amounts. Whereas, serum albumin alone may be present, this is hardly ever the case with globulin. The results of the investigations which have been carried out with a view to determining the significance of the relative proportions of the two proteins in albuminous urine have not proved of much clinical value. It would seem that a low proportion of globulin in cases of nephritis is a favorable indication. Haliburton suggests that, speaking generally, much globulin indicates a grave renal lesion. Further than this our knowledge does not allow us to go.

Considerable interest attaches to that protein of urine which is precipitated by the addition of dilute acetic acid to the diluted or undiluted urine in the cold. That this is not mucus, as was originally thought, was shown by the fact that when treated with mineral acids it yields no reducing substance, and for many years it was looked upon as nucleo-albumin. Morner arrived at the conclusion that this substance was in reality composed of compounds of serum albumin with chondroitin-sulphuric acid, nucleic acid, and, in cases of jaundice, with taurocholic acid. It has been stated by A. Oswald that the protein so precipitated from albuminous urine in cases of nephritis and of cyclic albuminuria is a mixture of euglobulin and fibrinogen. More recent work seems to prove that this substance is derived from the blood and is not a product of the diseased renal epithelium. Its presence has, therefore, a like significance to that of serum albumin and globulin.

In considering the clinical significance of albuminuria it is necessary

to draw a sharp distinction between the true renal forms and what has been styled accidental albuminuria. The mere presence of albumin in the urine does not necessarily imply a renal origin. In some cases it results from the admixture of vaginal discharge or of semen, in others it is due to disease of the urinary passages. Urine which contains blood or pus must always yield the reactions of albumin, and albumin is also present in chylous urines.

*Physiological or functional albuminuria* offers a problem of no small difficulty, upon which the last word has by no means been said. It may be taken as proved that minute quantities of albumin, so minute that they escape the ordinary tests, are present in normal urines. Somewhat larger amounts are not uncommonly met with apart from any other signs of organic renal disease. As a rule the albumin present in cases of functional albuminuria is precipitated to a greater or less extent by acetic acid in the cold. Some subjects of functional albuminuria excrete albumin only after exertion, others after a cold bath, and others after mental or bodily strain. Severe and prolonged exertion will induce albuminuria in many persons. Often the functional albuminuria is profoundly influenced by position, and may only be present during the active hours. However, the influence of posture is also well marked in cases of albuminuria due to gross renal lesions.

That the excretion of albumin in quantities easily detected is not strictly normal is an obvious truism, but the evidence is strong that it may be a symptom of no serious significance. Our interpretation of the observed facts will depend largely upon the views which we hold as to the limits of idiosyncrasy as distinguished from disease. A few such cases carefully watched from childhood to advanced life would throw more light upon the question than many investigations covering only brief periods.

*Albuminuria due to circulatory disturbances* is a common symptom, well exemplified in cases of cardiac disease in which compensation fails and backward pressure leads to passive congestion in the kidneys. It is uncertain how far the increased pressure is directly responsible for the escape of albumin under such conditions, but it seems certain that the main cause is a secondary change in the renal epithelium due to deficient conveyance of oxygen to the part. When there is a complete obstruction of the renal vessels, as the result of embolism or thrombosis, the necrotic changes in the infarcted area amply account for the albuminuria which results. The albuminuria of cholera has been ascribed to deficient blood-supply to the kidneys, but toxic influences probably play an important part.

In the *albuminuria of fevers*, which constitutes a well-defined variety, circulatory disturbances may also come into play, but it is probable that a mild form of toxemic nephritis is often produced, and the cloudy swelling, so often seen at autopsy, bears witness to the changes in the renal parenchyma which fevers induce. This view gains in probability from the observation that the duration of the fever, rather than its intensity, is the most important factor in determining the excretion of albumin.



Albuminuria of slight degree is a common symptom in *jaundice*, and here also it is presumably toxic. Hyaline casts are usually present in considerable numbers, even in cases of jaundice in which no albumin is to be detected by the ordinary tests. Graver varieties of *toxic nephritis* are caused by various poisons, such as cantharides, turpentine, and carbolic acid.

Special interest attaches to the albuminuria which is associated with nervous disturbances, the pathology of which is obscure. The temporary presence of albumin in the urine after epileptic fits, which has occasionally been observed, has been compared with that which is sometimes induced in healthy subjects by violent muscular exertion.

The albuminuria which results from *gross lesions of the kidneys* is the most important of all. The quantities of albumin excreted vary quite widely from the conditions met with in acute parenchymatous nephritis, and in many chronic cases of the same disease, in which the urine becomes almost solid on boiling, to the no less significant presence of mere traces, in association with granular kidneys. However, in cases of granular kidney in which the heart is beginning to fail the amount of albumin in the urine may be very greatly increased.

**Detection of Albumin in Urine.**—The tests most often employed in clinical work are the heat test and the cold nitric acid test. Although they are far from being the most delicate available it may safely be stated that any quantity of albumin which they fail to reveal may, for ordinary clinical purposes, be neglected.

In performing the heat test the urine, if at all turbid, should be filtered, and the upper portion of the column in the test tube should be boiled. If a turbidity appears this may consist of albumin or of earthy phosphates thrown down as a result of a rearrangement of bases produced by boiling. On the addition of a drop or two of acetic acid the cloud will disappear, if it be due to phosphates, but if albuminous will persist or increase in density. When much albumin is present the coagulum will collect together and become flocculent when the acid is added. Urines containing traces of albumin may show no turbidity on simple boiling, but if they be again boiled after the addition of acetic acid a cloud may appear. This second boiling should always be carried out. For the detection of slight turbidity the test tube should be held before a dark surface.

In many albuminous urines, turbidity is produced when acetic acid is added in the cold, especially if the urine has been previously diluted with water. This is the precipitate of euglobulin and fibrinogen which has been referred to already. Precipitates of urates similarly produced will clear on warming; they will not appear after dilution of the urine.

The advantage of the heat test lies in the fact that it is not yielded by other proteins than serum albumin and globulin. The only other urinary protein precipitated by heat is the Bence-Jones protein, but this is distinguished by the fact that coagulation begins at an unusually low temperature and that the liquid usually clears almost completely as the boiling-point is approached, especially if acetic acid has been added. The precipitate of earthy phosphates will hardly lead to mistakes, as acetic acid should always be added as a routine proceeding.

Heller's test with cold nitric acid is best performed as a contact test. If albumin be present an opaque white ring, or rather disk, appears at the junction of the liquids. Beneath it a colored layer is often seen, due to oxidation of indican. When very minute traces of albumin are sought for it is well to employ a wide test tube or a small beaker. A faint, hazy ring above the junction of the liquids is due to the protein which was formerly spoken of as nucleo-albumin. In concentrated urine a ring of uric acid may form, which disappears on warming and is not obtained after dilution of the urine. After standing for a short time a crystalline ring of nitrate of urea is formed if the urine tested be very concentrated. Another possible source of error is the precipitation of resins, such as copaiba, in the urine of patients taking such drugs. Other proteins, such as the Bence-Jones albumin and albumoses yield this test as well as serum albumin and globulin.

A number of different test solutions are also employed for the detection of proteins in urine. These all precipitate albumoses in addition to albumin and globulin, but the albumose precipitates disappear on heating, to reappear when the liquid is cooled. Of such reagents, a saturated solution of picric acid is often used, either as a ring test or by the addition of the urine to the test solution. Care must be taken that the reagent is in excess. A solution of potassium ferrocyanide is widely employed, after acidification with acetic acid. Trichloroacetic acid may also be mentioned, and salicyl-sulphonic acid, which is one of the most delicate and satisfactory of the precipitants of proteins; and only proteins are precipitated by this reagent. A few drops of a saturated solution of salicyl-sulphonic acid are added to the urine in the cold. If a turbidity results the liquid should be heated, when the turbidity, if due to an albumose, will disappear. The presence of globulin in considerable amount may be demonstrated by Sir William Roberts' test. The urine is allowed to fall, drop by drop, into a beaker of distilled water. If much globulin be present the path of each drop is made visible by a milky turbidity, for such proteins are insoluble in distilled water.

A very rough notion of the proportion of albumin present in urine may be obtained by boiling a specimen in a test tube after the addition of a drop of acetic acid, and estimating the relative depth of the coagulum after it has had time to settle. By the use of Esbach's albuminometer a much more accurate notion may be obtained which suffices for ordinary clinical purposes, such as the estimation of the progressive diminution of albuminuria during recovery from acute nephritis. For accurate determinations, either of the total albumin or of serum albumin and globulin separately, it is necessary to proceed by laboratory methods, the proteins being isolated from the urine, dried and weighed.

**Sediments Indicative of Disease in the Urinary Tract.**—The microscopic examination of urinary sediments often supplies important information as to the presence of morbid conditions in the kidneys or urinary tract. Normal urine is clear and limpid when passed, but on standing a slight cloud develops in the liquid, which is known as the nubecula; this may lie at the bottom or may hang suspended in the urine. The position is in part determined by the specific gravity of

the liquid and in part by the inclusion of air bubbles. The bulk of the nubecula consists of urinary mucoid, and in it are entangled a few epithelial cells, the sheddings of the surface layers of the mucous membrane, and also a few leukocytes. Seeing that, with the exception of bacteria, no cellular elements can pass the renal filter, any such which are present in the urine are derived from the kidneys themselves, or from the urinary passages, bladder, or generative organs. A few squamous epithelial cells may be looked upon as normal urinary constituents; only when the cells are numerous, and bear signs of coming from the deeper layers of the mucous membranes or from the renal tubules, can they be regarded as indicative of disease.

Red-blood corpuscles afford the sole criteria of hematuria as distinguished from hemoglobinuria, and their presence, even in small numbers, is evidence of hemorrhage from the kidneys or below. After soaking in urine they lose their hemoglobin and their biconcave form, and become globular or crenated. Leukocytes may be derived from vaginal secretion, and the presence of a few such cells has no serious import. In cystitis they may occur in any numbers, and when suppuration occurs in the kidneys or any other portion of the tract. The presence in them of gonococci is naturally of prime diagnostic importance. In alkaline urines they are apt to be swollen, globular, and hyaline, and their nuclei may only be demonstrable by the addition of acetic acid. When, as is sometimes the case, it is difficult to distinguish the leukocytes from cells from the renal tubules, the far deeper staining which iodine imparts to the former may be employed as a test.

The epithelial cells which are met with in urine are of different shapes and sizes, and from their characters some indication may be obtained of the parts from which they are derived. However, even to the trained eye the exact determination of their place of origin presents no small difficulty, especially when, as is often the case, they exhibit degenerative changes which alter their appearance and forms. The cells shed from the surface layers are usually of the flat varieties. Exceptionally large squamous cells, often adherent into groups, are derived from the mucous membranes of the vulva, vagina, and prepuce. Of the true urinary epithelial cells those from the bladder are the largest. Tailed, pyriform, and oval cells are derived from the deeper layers and therefore suggest a more deep-reaching affection. They may come from the bladder, prostatic urethra, or pelvis of the kidneys. The small, rounded, or polygonal cells, with well-defined nuclei, which are derived from epithelium of the renal tubules, are the most important from a diagnostic standpoint, and if abundant they afford evidence of renal disease hardly less convincing than that derived from the presence of renal casts. Not merely the presence but also the condition of the epithelial cells is of importance. Some changes are merely due to their being soaked in the urine, but the presence of fat globules in their protoplasm may serve to give an idea of the stage of the morbid process at their place of origin.

**Renal Casts.**—These owe their importance to the fact that, being obviously formed in the renal tubules, their presence in any considerable numbers indicates that all is not well with the kidneys; and that when



albumin or blood is also present the albuminuria or hematuria is of renal origin. The evidence of their renal origin is conclusive. In shape and size they correspond to the renal tubules, and they are often bedecked with epithelium which is obviously renal. Moreover, in sections of diseased kidneys they are frequently seen in situ. However, it cannot be inferred from the presence of a few hyaline or stippled casts in a centrifugalized deposit that anything serious is amiss with the kidneys. A few such objects may be found in some otherwise normal urines if the centrifuge be employed, and the almost constant presence of such casts in cases of jaundice suggest an irritant action of the bile constituents in the circulation upon the renal epithelium. Of renal diseases, it is in those which specially implicate the renal parenchyma that casts are most numerous, whereas in granular kidney they are scanty or absent.

*Hyaline casts* are very delicate structures, so transparent that they may be difficult of detection in unstained specimens. Such casts vary greatly in length and often have broken ends, indicating that they originally formed parts of longer specimens. It would seem that hyaline casts often indicate the slightest degree of renal mischief or the incipience of graver troubles. They are usually abundantly present in the early stages of acute nephritis, but even in the most chronic cases of parenchymatous nephritis they are met with in association with casts of various other kinds.

*Epithelial casts* are considerably larger than the hyaline, as is natural, seeing that the former correspond in size to the lumen of the renal tubule, whereas the latter represent the size of the tubule stripped of its epithelial lining. Every stage is met with, from a hyaline cast with a few cells from the tubal epithelium attached to it, to those which apparently consist wholly of epithelial cells, or from which a bare hyaline core may project at one end. Such objects are seen in their most perfect forms in the early days of an acute nephritis, and the cells with which they are clothed may have a cloudy or swollen appearance. Later on the condition of the epithelial cells may bear witness to a more advanced stage of disease; they may have a granular appearance, or may even contain highly refractive fat globules.

The so-called *amyloid* or *waxy casts*, larger and less transparent than the hyaline, but homogeneous and often showing partial segmentation, are believed by many to be derived from those of the epithelial variety by degeneration and fusion of the constituent cells. Although they sometimes show the red coloration with methyl-violet and stain deeply with iodine, their presence affords no evidence that the kidneys from which they come are lardaceous. They indicate rather an advanced and chronic renal trouble, and are most often met with in cases of chronic parenchymatous nephritis of somewhat long standing.

The casts which are grouped together under the name of *granular* differ considerably in appearance and size. Some are narrower and some broader; the component granules may be larger or smaller in size. They are opaque objects, and often have a brown tint. That they are friable is shown by the fact that they are usually short and often show broken ends. It is believed that the granules arise from the disintegration

of epithelial cells, and they are therefore held to indicate somewhat advanced renal lesions. They are met with in the urine in all varieties of nephritis and a few may be present in cases of granular kidneys. In cases of chronic parenchymatous nephritis a large proportion of the casts present are usually of this nature. Transitional stages between epithelial and granular casts are not infrequently met with.

*Fatty casts* are held to denote an advanced degeneration of the renal epithelium. Fat granules, recognized by their high refractive power, are sometimes present in the cells of which epithelial casts are composed. In many granular casts some of the granules are composed of fat, and occasionally the casts are mainly composed of fat globules. Acicular crystals of fat or of fatty acids sometimes project from such casts, usually from one extremity, and impart a hedgehog appearance.

Among other varieties, hyaline casts studded with red-blood corpuscles or crystals of calcium oxalate are sometimes seen. Casts richly beset with red corpuscles are common in the early stages of acute nephritis. Leukocyte or pus casts are much less common, as also are such as are composed of bacteria.

The so-called *cylindroids*, long hyaline objects with tapering ends which often show a wavy outline and longitudinal striation, are threads of mucus which have no connection with true renal casts. Other objects which simulate renal casts are composed of amorphous urates or of hemoglobin debris which have assumed cast-like forms.

Spermatozoa must also be mentioned among objects found in the sediment. Their presence will sometimes explain a slight albuminuria, and deprive it of any import as a sign of renal trouble.

The presence in the sediment of the ova of *Bilharzia hæmatobia* will afford conclusive evidence in cases of endemic hematuria. Within the oval envelope with its lateral or terminal spine the ciliated embryo is visible, and sometimes makes its escape from the shell under observation. The presence of hydatid hooklets which are easily recognized by their characteristic form, or of scolices, reveals the presence of hydatids in, or in connection with, the urinary tract; and the *Filaria sanguinis hominis* has sometimes been found in the urine.

Hairs are usually accidental additions, but when a teratoma communicates with the tract hair is sometimes passed in considerable quantities, the phenomenon being known as *pilimictia*.

**Crystalline Sediments.**—Although their presence is usually dependent upon processes behind the kidneys, they may afford valuable clues as to the nature of a calculus or gravel, the presence of which is indicated by other symptoms. The various crystals have very different degrees of diagnostic value. Thus, whereas the presence of hexagons of cystin is the diagnostic sign of cystinuria, and renders it almost certain that symptoms of calculus are due to cystin stone or stones, other crystals such as those of phosphates indicate little more than an abnormal reaction of the urine, and those of triple phosphate suggest ammoniacal decomposition. It is a matter of no small importance whether the crystals are already present in the urine when it is passed, or merely separate when it is allowed to stand.

*Uric acid crystals* are the commonest of all those met with in urine. They are always tinted, although sometimes very faintly, by included urinary pigments. In carboluria the uric acid acquires a deep brown color, and the crystals appear black when seen in bulk. Those deposited from bile-stained urines are colored by the bile pigments, and when biliverdin is present are grouped into rosettes of greenish-yellow prisms. The exact conditions which determine the deposition of crystalline uric acid are not fully known. Klemperer assigns much importance to scantiness of urochrome; acidity certainly plays a part, as also does the amount of uric acid present, although excessive output of uric acid can by no means be assumed from the deposition of crystals.

Crystals of *ammonium urate* are not infrequently deposited from feebly alkaline or amphoteric urines, often in company with those of ammonio-magnesium phosphate. Sometimes they assume the form of minute yellow dumb-bells or of the so-called "hedgohog crystals," small yellow spherules with sharp excrescences.

*Calcium oxalate crystals* are, next to those of uric acid, the commonest of all. They are often very minute, and form a snow-like layer on the top of the nubecula, or adhere to grease marks upon the sides of the containing glass. The commonest form is a flat octohedron which appears under the microscope in the semblance of a square envelope. Less common are cubical prisms with pyramidal ends. Twin crystals composed of interpenetrating octohedral forms are also seen. Imperfectly crystalline forms are sometimes present, such as oval disks with deep central grooves upon their flat surfaces and more rarely true dumb-bells. When deposited from bile-stained urine, crystals of calcium oxalate are faintly tinted by bilirubin or biliverdin.

*Ammonio-magnesium* or *triple phosphate* is deposited in crystalline form from any urine which is undergoing ammoniacal decomposition, and the presence of such crystals has no greater significance than this. They assume various forms, of which the most characteristic is the familiar "knife-rest" or "coffin-lid" shape. Feathery forms are also met with. When the urine is frankly alkaline they are usually surrounded by a deposit of amorphous earthy phosphates, which, with the crystals, are easily soluble in acetic acid.

*Neutral calcium phosphate* or "stellar phosphate" forms crystals which are easily recognized and are not seldom seen in amphoteric urines and in those which owe their alkalinity to fixed alkalis. They form long, wedge-shaped prisms, with their broader ends cut off obliquely. They are usually grouped into stars, with their pointed ends toward the centre of the star.

*Magnesium Phosphate*.—In some forms of gastric disorder treated by large doses of magnesium carbonate, tabular crystals of normal magnesium phosphate have been met with in the urine.

*Crystals of cystin* are among the rarest of urinary sediments. They form colorless hexagonal plates the sides of which are often of unequal lengths, and groups of superposed hexagons are common. They may be distinguished by their ready solubility in ammonia and also in hydrochloric acid.



*Xanthin crystals*, which are always described among urinary sediments as lemon-shaped and yellow in tint, have been met with in only a single case, described by Bence-Jones many years ago, and were only present for a day or two.

*Calcium sulphate* has been rarely met with as a sediment composed of long needles or tables with sloping ends; *calcium carbonate* is sometimes deposited from alkaline urines in small dumb-bells or spherules with concentric striation. *Calcium and magnesium soaps* in crystalline form, as needles resembling those of tyrosin, for which they may readily be mistaken, have been described by von Jaksch, and are sometimes seen adhering to and projecting from fatty casts.

*Bilirubin or hematoidin*, in the form of minute brown acicular crystals, may be found in urines containing bile, and in some cases of malignant disease of the kidneys or urinary tract in which old extravasations of blood are breaking down. Crystals of these substances are indistinguishable from each other and probably are chemically identical.

*Hippuric acid* has been rarely seen as a urinary sediment composed of rhombic prisms.

*Indigo blue* is found in amorphous particles in many alkaline urines, and rarely in the form of crystals.

*Crystals of tyrosin and leucin* will be described elsewhere.

In connection with disease in the urinary tract, *deposits of crystalline cholesterin* are of special interest, although they are very rare. The crystals may be very abundant, so that they appear as innumerable glistening particles when the urine is shaken. They have the characteristic form of rectangular plates each with one corner removed. The excretion of crystalline cholesterin has been observed in association with a variety of morbid conditions, all of which have this in common, that they are characterized by local lesions in the urinary tract. Thus, it has occurred in cases of congenital cystic disease of the kidneys, hydronephrosis, pyonephrosis, and chronic cystitis of long standing. Plaques of crystalline cholesterin have been found postmortem on the inner surface of the bladder and of the renal pelvis, and even in the substance of the kidney.

Lastly, calculi chiefly composed of cholesterin have occasionally been passed or removed from the bladder. These have usually been gall-stones which have found their way into the urinary passages through bilio-urinary fistulæ, as was shown by the presence of bilirubin calcium, by faceting in some instances, or by the excretion of deeply bile-stained urine apart from any jaundice. No such explanation can be given, however, of a large calculus of almost pure cholesterin, described by Horbaczewski, which was removed by suprapubic lithotomy from the bladder of a little girl, and was mistaken for a cystin stone.

**Hematuria.**—Among the symptoms which indicate disease of the kidneys or urinary tract hematuria claims an important place. In many cases the diagnosis of the place of origin of the admixed blood, and of the cause of hematuria, presents little difficulty; in others both are extremely obscure. Whether the blood comes only at the beginning of micturition, or only at its end, or whether it is intimately mixed with

the urine, are points which afford valuable aid. Again, cystoscopic examination or the use of the separator is often of great use.

The microscope not only supplies the only certain means of diagnosing hematuria from hemoglobinuria, a symptom of wholly different significance, but may also throw much light upon the origin of the blood. Thus the presence of numerous casts, and their characters, will serve to locate the lesion in the kidneys, and may show whether we have to do with an acute lesion or with one of a more chronic kind. Again, detached epithelial cells, if present in considerable numbers and of characteristic forms, may serve to indicate the situation of a lower lesion. The presence of crystals of certain kinds in considerable numbers lends color to the view that the hematuria is due to a calculus, whereas the presence of many crystals of calcium oxalate is equally compatible with that form of hematuria which results from the free consumption of rhubarb. The mere fact that red corpuscles are the only objects to be detected in the sediment is of no slight clinical value in particular cases, in excluding some of the causes of hematuria.

Apart from the microscopic test, the tests for hematuria are mere indications of the presence of blood pigment as distinguished from blood. Urine containing blood necessarily yields the tests for albumin, and the negative results of such tests may exclude the presence of blood in cases in which the appearance of the urine suggests hematuria. On the other hand, the presence of an amount of albumin out of all proportion to the hemoglobin strongly suggests a renal origin.

The *color* of the urine differs widely in different cases. It may resemble that of pure blood when the hemorrhage is copious, or a considerable sediment of blood may form on standing. When less blood is present it may impart a pink tint, or the urine may appear brown and smoky. The color may change from brown to pink on standing in contact with air. The brown tint is usually due to methemoglobin, but occasionally a deeply brown-stained sediment contains the pigment in a peculiar insoluble form, whereas the yellow supernatant liquid fails to yield the tests for hemoglobin. Alkaline urines containing blood have a peculiar livid tint in their deeper layers, shown by the spectroscope to be due to reduction of part of the dissolved hemoglobin.

If the blood pigment in urine were always in the form of oxyhemoglobin the spectroscopic test would be a very delicate one, but the band in red of methemoglobin is not readily seen in very dilute solutions. In some cases of hematoporphyrinuria the pigment is in metallic combination, and shows absorption bands which may easily be mistaken for those of oxyhemoglobin. When such urines contain albumin in small amount, the risk of mistake is much greater than when they are albumin-free.

Hellers' test, by boiling the urine with liquor potassæ, is a delicate one, and when, after boiling, the color of the stained phosphate precipitate changes from brown to pink, and shows the spectroscopic bands of hemo-chromogen, the presence of blood pigment is placed beyond doubt. It must be remembered that chrysophanic acid, present in the urine of patients taking rhubarb and senna, also tints the phosphate sediment deeply, but sediments so tinted show no distinct absorption bands.

The guaiacum and ozonic ether test is a very delicate one, provided that the reagents are freshly prepared. Under such conditions a negative result excludes the presence of blood pigment, and in practice the fact that other substances than blood cause the development of a similar blue color will seldom mislead. The most likely cause of error is an iodide, taken as a drug, but unless the iodide be present in very large amount the blue color appears much more slowly than in urine containing more than minimal traces of hemoglobin. To the trained eye the appearance of the urine affords as delicate an indication as any of the presence of blood pigment but confirmatory tests are of course essential.

The *causes* of hematuria are numerous. The blood may come from any part of the urinary tract, as the result of a variety of lesions. Thus, hemorrhage from the urethra may result from external injury, the passage of a calculus or gonorrhœa; the blood is passed at the commencement of micturition. Prostatic hemorrhage is not uncommon. Blood may come from the bladder in cystitis, when a calculus is present, or when its walls are the seat of tuberculous ulceration or of villous growths. In the vesical group may also be included the hematuria due to *Bilharzia hæmatobia*, and that of chyluria. Hemorrhage from the ureters may result from the passage of a calculus or from tuberculous ulceration, and to the same causes, as also to new growths, may be due hemorrhage from the renal pelvis.

Renal hematuria has many different causes. In acute nephritis blood is almost always found in the urine, and in unfavorable cases the hematuria persists into the chronic stage. Copious hematuria occasionally results from granular kidney. In lardaceous disease it is not a prominent symptom and is usually absent. Laceration of the kidney gives rise to copious renal hemorrhage. In renal tuberculosis hematuria is sometimes a prominent symptom, as also when the kidney is the seat of malignant growth. Infarction, if extensive, usually causes blood to appear in the urine. Among poisons, some, such as turpentine and cantharides, produce acute nephritis with hematuria.

Hematuria may occur in such diseases as purpura hemorrhagica, leukemia, or scurvy, and also in the course of hemophilia. In infantile scurvy hematuria of slight degree is a very common symptom, and may be the first to attract attention.

Certain less well recognized and more obscure varieties of hematuria call for special mention. Crystals appear to be capable of causing hemorrhage by the mechanical effect of their passage. Uric acid crystals may produce this result in young infants, and even in adults calcium oxalate crystals have this power. In a not uncommon form of hematuria, which is alarming but without serious import. The excretion of blood and of numerous oxalate crustals is due to the copious eating of vegetables rich in oxalate. Of such rhubarb is the chief offender.

Far more obscure are certain cases of renal hematuria, which may be so copious as actually to threaten the life of the patients, but which are due to none of the causes enumerated above. The blood usually comes from one kidney, as is shown by cystoscopic examination, and in some instances nephrotomy has been performed, the kidney split



open and no lesion found; yet after the operation the hematuria has permanently ceased. It is to such cases that the terms "renal hemophilia" and "renal epistaxis" have been applied. In some such cases Hurry Fenwick has observed a dilatation of the vessels of a single papilla, removal of which has cured the hematuria, and microscopic examination of the part removed has revealed localized interstitial change.

**Pyuria.**—When accidental admixture can be excluded, the presence of pus in the urine affords important evidence of a lesion in or in connection with the urinary tract. The appearance of urine containing pus depends upon the quantity present and upon its reaction. From acid urine the pus tends to settle as a dense deposit of a yellowish or greenish hue, whereas the supernatant urine is clear. In alkaline urine the deposit is stringy and less circumscribed, and tends to cling to the sides of the containing vessel. Numerous epithelial cells accompanying the leukocytes may give an indication of the seat of the mischief. The time-honored teaching that pus in acid urine is usually of renal origin, whereas alkaline urine containing pus indicates a vesical lesion, often holds true, but the reaction of the urine is mainly dependent upon the nature of the infective organism at work in producing the pyuria; and whereas in cystitis due to *Bacillus coli* the urine tends to remain acid, the organisms of the *proteus* group may cause pyelitis by extension, and pyuria with alkaline urine.

The pus present in the urine may have its origin in a purulent urethritis, usually gonococcal, but sometimes due to other organisms. Cystitis is always accompanied by pyuria, which may be of any degree from the presence of a few leukocytes upward. Tuberculous disease of the kidneys is an important cause of pyuria, and in such cases the urine is acid, unless there be a mixed infection. Pyelitis by extension and calculous pyelitis are also attended with pyuria. In pyonephrosis the discharge of pus is apt to be intermittent, and when an abscess in a neighboring part opens into the urinary passages there is usually a copious discharge of pus for a time, followed by a more or less rapid cessation of the pyuria. Urines which contain pus are necessarily albuminous, but the presence of an amount of albumin out of all proportion to the pus offers a strong presumption of a renal origin.

Of the tests for pus in urine microscopic examination is the most conclusive. The ropy condition produced by the addition of a caustic alkali is often of value. When a layer of ozonic ether is poured upon the top of the urine in a test tube, and gently shaken with it, streams of oxygen bubbles rise through the ethereal layer if the urine contains pus; but as Dixon Mann explains, this test fails to discriminate between true pyuria and mucus derived from the urinary mucous membranes.

When purulent urine is passed through a filter paper the pus left upon the filter yields a blue color with tincture of guaiacum, without any addition of ozonic ether or other oxidizing agent. In performing this test care should be taken that the filter paper used does not itself yield a blue color with the reagent.

**Chyluria.**—The passage of chylous urine indicates the opening of a lymphatic vessel into the urinary passages. This event is usually due

to the presence of the *Filaria sanguinis hominis*, but there are cases met with in patients who have never resided in a tropical climate, in whom the presence of chyluria cannot be ascribed to any parasitic cause.

The excretion of the chylous urine is usually intermittent, and is determined by such causes as the taking of food and the posture of the body. The fat which imparts the milky appearance is in extremely fine division, the minute particles being far smaller than the fat globules in fresh milk. The microscopic appearances are more nearly imitated by mixing condensed milk and water. That the opacity is due to fat may be shown by shaking the urine with ether. The fat dissolves in and is separated by the ether, whereas the subjacent urine is left clear or only slightly turbid.

Chylous urine sometimes sets into a jelly after it is passed, but after a short time liquefies once more. Occasionally the setting occurs in the urinary passages, with distressing results. Albumin and albuminoses also occur in chylous urines, and the presence of blood often imparts to it a pink tint.

**Fibrinuria.**—In rare instances the urine has been observed to form jelly-like masses after it was passed, apart from the presence of chyluria. This phenomenon has sometimes been associated with grave forms of renal disease with highly albuminous urine. When hemorrhage occurs into the urinary passages fibrin is also, of necessity, excreted, and clots may form in the bladder or elsewhere.

**Pneumaturia.**—The passage of gas bubbles with the urine, which is sometimes attended with a clearly audible sound, may arise from two wholly different causes. In some cases the gas finds its way into the bladder from the lower intestine, passing through a fistulous opening which is usually a result of a malignant growth with ulceration. Passage of fecal particles and debris per urethram will confirm the diagnosis of perforation. True pneumaturia, on the other hand, is a sign of infection of the bladder, and the liberation of large quantities of gas by bacterial action. If only a small quantity of gas be formed, it will be rapidly absorbed and will not pass as such. In the great majority of cases the symptom is associated with diabetes, and the gas expelled is carbon dioxide, liberated by the fermentation of glucose within the urinary tract. However, this is not always the case, and Adrian and Hann have described a class of cases in which glycosuria is absent, and the gas is formed by the action of bacteria of the colon group or *Bacillus lactis aërogenes* upon proteins in the urine of patients with cystitis.

#### ABNORMALITIES OF THE URINE DUE TO DISORDERS BEHIND THE KIDNEY

Almost any disturbance of the metabolic processes of which the body is the seat will induce deviations from the normal in the urine. Some such deviations are very inconspicuous and not easy of detection, others are obvious and do not require to be looked for.

**Polyuria and Ischuria.**—Some variations in the quantity of urine excreted may be classed as physiological, such as the increase due to

copious drinking of liquids, and the decrease with profuse sweating; individual peculiarities play an important part in determining the volume of the urine or, more strictly speaking, the amount of liquid ingested.

The influence of diuretic drugs and beverages must be taken into account, and the profound influence of the nervous system, which reaches its limits in the polyuria of fright on the one hand and hysterical anuria on the other. Among morbid conditions there call for special mention the ischuria of fevers and the polyuria which is a common symptom of convalescence from these, the polyuria which accompanies the absorption of dropsical effusions, the ischuria of diarrhoea, and the excessive polyuria of diabetes mellitus and diabetes insipidus. The influence of renal disease upon the quantity of urine is discussed elsewhere.

**Color of the Urine.**—This is the most obvious of its characters, and the changes which it undergoes in disease have been recognized as of diagnostic value since the days of Hippocrates and Galen. For clinical purposes urines may be conveniently classed as: (1) Yellow and orange; (2) pink and red; (3) brown and black; and (4) green and blue. Abnormalities of tint may be due to changes in the relative amounts of the pigments which may be strictly classed as urinary, to the presence of body pigments which are not normally excreted by the kidneys, or to pigments derived from articles of food or drugs.

**Yellow and Orange Urine.**—The yellow tint of normal urine, which varies in depth with its concentration and with the amount of pigment excreted, is due to urochrome, for the other normal pigments are present in quantities so minute that they have no obvious coloring effect. There is little doubt that the amount of urochrome is materially affected by disease, but we have no exact knowledge of these variations, nor, indeed, of where this pigment is formed. Urines rich in urobilin show the dark absorption band of that pigment situated near the solar F line, and have a richer orange tint than normal urine. Whereas, urochrome retains its yellow tint on dilution so long as any color remains visible, very dilute solutions of urobilin have a pink hue, and when urine rich in this pigment is examined in a conical glass, a pinkish tint is visible at the apex of the cone. Uro-erythrin in solution imparts a fiery orange tint, which may even suggest the presence of blood, whereas urate sediments colored by it are pink in color.

Certain drugs modify the yellow color of urine. Chrysophanic acid, which is contained in rhubarb and senna, has this power, as also has santonin. In both instances the color of the urine is changed to pink by the addition of an alkali. A small admixture of bilirubin imparts a brownish-orange tint.

**Pink and Red Urines.**—The commonest cause of a pink or red color of urine is the presence of oxyhemoglobin, but when the quantity of blood pigment is scanty it is usually changed to methemoglobin and imparts a smoky tint. In the condition known as hematorporphyrinuria, which will be discussed later, the color of the urine varies from that of port wine to absolute blackness, but the small amounts of hematorporphyrin which are present in various morbid conditions, although they may greatly exceed the normal traces, do not appreciably modify the



color of the urine. Rosanilin, when administered as a drug, renders the urine pink, and eosin, contained in certain sweetmeats, also imparts a pink color, which is accompanied by a brilliant green fluorescence. To alkaline urine chrysophanic acid may impart a deep pink color.

**Brown and Black Urines.**—Various causes may give rise to such coloration, and the associated conditions differ widely in gravity. Urines rich in bile pigment, and especially those in which some biliverdin is present, often approach to blackness, and the same is true of some which contain blood or hemoglobin. Methemoglobin, even in small amounts, imparts a brown or smoky hue, and it is probable that many of the black urines of early writers belonged to this class. Some were almost certainly passed by patients with paroxysmal hemoglobinuria, and the name of “black-water fever” bears witness to the production of blackness by altered hemoglobin. In some cases of hematuria also the urine may fairly be described as black.

In some cases of *indicanuria* the urine darkens on standing, and becomes dark brown or even black. The color is not due to the indoxyl sulphates, which are colorless, but to higher oxidation products of indol. This variety of dark urine is not so well recognized as it should be, and it is probable that the condition in question has occasionally been mistaken for melanuria. When such urines are warmed with nitric acid, blackening results; and when Jaffe’s test for indican is carried out, chloroform takes up abundance of purple pigment, indigo blue and red, whereas the supernatant liquid remains as black as before.

In true *melanuria*, indicative of widespread melanotic sarcoma, the urine is usually of normal color when passed, very seldom brown. On exposure to air it darkens from the surface downward, becoming first brown and later absolutely black.

The darkening of alkapton urines on exposure to air follows a very similar course, but the two conditions are easily distinguished.

Some drugs cause the secretion of urine which blackens on exposure to air; thus, carboloria is a familiar phenomenon which is ascribed to the excretion of hydroquinone, and among other drugs which produce like effect may be mentioned naphthalene, salol, creosote, thallin, and, to a less degree, salicylates. The leaves of *uva ursi* contain arbutin, from which hydroquinone is formed, and this may cause a conspicuous darkening of the urine of patients taking that drug.

**Green and Blue Urine.**—Urines which contain bile pigment almost wholly in the form of biliverdin have a deep green color, but with this exception it may be stated that practically all green urines, as well as those which have a blue color, owe their tints to methylene blue. Anyone familiar with the reactions of such urines can easily convince himself of the nature of the coloration, but it is not always easy to ascertain how the methylene blue was introduced into the alimentary canal. Sometimes it has been administered as a drug, and the cause of the phenomenon is obvious; sometimes it has been taken in sweetmeats, and it should be mentioned that some white sweets contain it. Sometimes, again, one is driven to the conclusion that a pill of methylene blue has been introduced accidentally or otherwise among those of a different kind which

the patient is taking. This much is certain, that until coloration by methylene blue can be definitely excluded, speculation as to the nature of a green or blue urine is wasted.

**Hematoporphyrinuria.**—Among conditions which are characterized by abnormal pigmentation of the urine this calls for special mention. It usually results as one of a group of toxic symptoms from the taking of sulphonal, much more rarely of trional, over long periods. Hematoporphyrinuria may develop after a few doses of the drug, or only after it has been taken for several years in uniform nightly doses. It may even appear some days after the drug has been discontinued. Under any of these circumstances its prognostic significance is grave.

It is a remarkable fact that, whereas the group of symptoms of which hematoporphyrinuria is one have been observed in a large number of female patients, it has very seldom been seen in males. It will be well to limit the application of the term to cases in which the urine assumes a deep red color like that of port wine, or is even nearly black, and is found to contain quantities of hematoporphyrin which are far in excess of those usually present in urine. Normal urines contain minute traces of hematoporphyrin in a variety of morbid conditions, and especially in chronic lead poisoning the normal traces are considerably exceeded, but the tint of the urine is not materially altered thereby. In cases of hematoporphyrinuria, in the restricted sense, the dark color of the urine is not due to the pigment in question, but, as Hammarsten pointed out, to other abnormal pigments which accompany it of which little is yet known. The color of such urine cannot be simulated by the addition of hematoporphyrin, and when this pigment can be separated from the dark urines their color is not materially affected by its removal.

The absorption spectra of hematoporphyrin are complex and very characteristic, and the bands are dark and sharply defined. Yet in these urines its detection by means of the spectroscope is by no means so easy as might be expected. The pigment often existing in them is the so-called "metallic" form, that is to say, in a combination in which it shows two bands which closely resemble those of oxyhemoglobin.

The quantity present varies greatly, and it is sometimes necessary to precipitate the pigment before a certain diagnosis can be made. This may be done by the addition of calcium chloride and lime water, Salkowski's method. The precipitate, which carries down all the abnormal pigments, is extracted with alcohol to which sulphuric acid has been added, and the acid-alcoholic extract will show the spectrum of acid hematoporphyrin.

Hematoporphyrinuria may be suspected when urine is excreted which resembles port wine in color, which shows absorption bands resembling those of hemoglobin, but contains no albumin and does not give the guaiacum test for blood. Sometimes the mere addition of an acid brings out the characteristic spectrum of acid hematoporphyrin. If the patient has recently taken sulphonal the condition is at once explained. The drug should be stopped, and sodium bicarbonate should be given in large doses.

Very rarely hematoporphyrinuria has been met with apart from the administration of sulphonal or its allies. Under such circumstances the symptom is of no such evil omen, and there is no special liability of the female sex. The symptom may persist for years, may recur at intervals, or may assume a paroxysmal form resembling paroxysmal hemoglobinuria, as in a case recorded by Pal. In some cases the urinary anomaly has recurred in association with attacks of *hydropoæstivale*.

**Urobilinuria.**—Urobilin, which is recognized in urine by its dark absorption band near the solar F line, is mostly excreted in the form of a chromogen, which becomes converted into the pigment after it is excreted. Urobilin is mainly formed by the action of the intestinal bacteria upon bilirubin, and the bulk at least of the urobilin of urine is absorbed from the alimentary canal—whether there is not another source of the pigment within the body is a question which is not yet finally settled. The conditions which bring about an increased excretion of the pigment or its chromogen in the urine are multiple, and this deprives its presence of much of the clinical significance which it would otherwise possess. Mere constipation may lead to urobilinuria. Excessive hemolysis of moderate degree, with consequent pleochromia of the bile, is a well-recognized cause, and urobilinuria is to be expected in cases of pernicious anemia. In some cases an excessive urobilinuria has been observed as a result of the taking of trional, and in fevers of various kinds the urine frequently shows a strong urobilin band.

The influence of the liver upon the excretion of urobilin is beyond question, and urobilinuria is common in association with hepatic disease, an association the nature of which is difficult of explanation. After an attack of obstructive jaundice, while the skin is still yellow, although bile is again entering the intestine, the bile pigment tends to be replaced in the urine by a copious excretion of urobilin, and the term urobilin jaundice has been frequently employed. It should be mentioned, however, that there is no evidence that pigmentation of the skin and other tissues is ever due to the presence in them of urobilin in place of the unaltered bile pigment.

**Uro-erythrinuria.**—The frequency of pink urate sediments bears witness to the frequent presence of uro-erythrin in the urine in considerable quantities. This very unstable pigment has a great power of coloration. Of the material from which it is formed and of its place in the classification of pigments nothing is known. It is probably not a constituent of strictly normal urines, but even a slight digestive disturbance may cause it to appear. In fevers it is common, but all the clinical evidence available connects its presence in the urine with functional derangements or organic disease of the liver. Patients whose urine deposits uratic sediments of a deep pink color almost invariably have some hepatic trouble which is manifested by other signs, whether it takes the form of cirrhosis or of malignant tumors, or of the nutmeg change which results from circulatory derangements with backward pressure and chronic congestion. When no uratic sediment falls, the pigment, if abundant, imparts to the urine a fiery orange color, which is changed to a dirty greenish tint by the addition of an alkali.



**Indicanuria.**—Indoxyl is met with in urine mainly in combination with sulphuric acid, as the so-called urinary indican—a substance which is wholly different in nature from the indican of plants, which is a glucoside. A small fraction is in combination with glycuronic acid, and it is probably as the result of the spontaneous decomposition of indoxyl glycuronates that deposits of free indigo blue are sometimes formed in alkaline urines.

Even in health the protective mechanisms which lead to the formation of such compounds, and so render the indoxyl harmless, are called into play to a small extent, and indoxyl-sulphates contribute to the normal quatum of aromatic sulphates. The parent substances of the urinary indican are the proteins of the food, which are in part decomposed in the intestine by bacteria. The particular portion of the protein molecule from which the indol is derived is the tryptophane fraction.

In many morbid conditions, and in some which can hardly be called morbid, such as simple constipation, the formation of indol in the intestine and the excretion of indoxyl compounds in the urine is conspicuously increased, and such increase may be interpreted as a measure of bacterial decomposition in the alimentary canal. That in the great majority of cases the increased excretion has this significance seems certain, although we cannot be sure that some of the indol formed does not undergo further changes in the tissues, so that the excretion of indigo precursors does not necessarily afford an accurate measure of the process. Indicanuria has sometimes been observed in cases in which the cavities of the body contained fetid pus, as in fetid empyema, and such collections may afford other sources of indol. Indicanuria is a very marked feature in melancholia and malignant disease of the liver.

In testing for indican it is essential that a freshly voided specimen of urine be used, as indican rapidly disappears on standing and so renders the results inconclusive. When urines containing indican are boiled with hydrochloric acid, to which a trace of nitric acid or of bleaching powder solution has been added, they undergo conspicuous darkening, and indigo pigments are formed. If hydrochloric acid be alone used indigo red is formed in excess; the oxidizing agents favor the formation of indigo blue. If they be added in too large quantities, isatin is formed and the result of the test may be deceptive.

If, after cooling, the acid liquid be shaken with chloroform, the chloroform acquires a deep purple color from admixture of the red and blue pigments, and with the spectroscope the absorption band in red, due to indigo blue, may be observed. If the chloroform be evaporated the two pigments may be separated by washing the residue with alcohol, which takes up the indigo red; whereas the indigo blue which remains undissolved forms a blue solution in chloroform.

**Melanuria.**—The excretion of melanin, or rather of its chromogen melanogen, in the urine is a sign of great diagnostic value as indicating the presence of a disseminated melanotic growth. In cases in which the tumor is still limited to its primary seat no melanuria is observed. Only when secondary tumors are forming is melanogen excreted, and the occurrence and intensity of the melanuria appear to be chiefly determined by the invasion of the liver.

The urine has usually the normal color when fresh but quickly darkens on exposure to air and ultimately becomes black. Occasionally it has a brown color when passed. The addition of nitric acid in the cold causes immediate blackening, as also does that of a solution of ferric chloride. This latter reaction is the most satisfactory of all, for it is not obtained in any of the other conditions which simulate melanuria more or less closely. Unless it is obtained melanuria should never be diagnosed, but in the early stages, while the amount of melanogen excreted is small, the blackening may only be partial. Bromine water produces a yellow or chocolate-colored precipitate which rapidly blackens (Zeller's test). Von Jaksch has also pointed out that the urine in melanuria yields a deep Prussian-blue color when sodium nitroprusside and potassium hydrate are first added and acetic acid is afterward added in excess. However, this test is yielded by other than melanin urines, and even in the cases under discussion is not to be attributed to melanogen.

**Lithuria.**—The deposition of amorphous sediments of urates as the urine cools is a very common event, and it cannot be too strongly insisted that this must not be interpreted as a sign that the daily output of uric acid is in any way above the normal limits. It often results from mere concentration of the individual specimen, due to excessive loss of water by the skin, as after violent exercise. Various factors contribute to the formation of such sediments, such as the degree of acidity of the urine, and an excessive output is one of these contributory factors. Even the temperature of the air has a potent effect, and uratic deposits are therefore more often seen in winter than in summer. Clinically, uratic deposits are common in the urine of patients with fevers and of sufferers from gout and various liver diseases. Their color varies from a pale yellow tint, due to included urochrome, to a deep pink, due to combined uro-erythrin.

This clinical association with gout has no relation to the excess of uric acid in the blood. The many investigations of recent years upon the urine of the gouty have failed to show any constant excess or decrease of the uric acid beyond the somewhat wide normal limits. Only just before the acute attack of gout has a diminished excretion been demonstrated, followed by an excessive output as the attack subsides.

A diet rich in purin substances, as in thymus feeding, causes a conspicuous increase of the excreted uric acid, and of morbid conditions the most obvious increase occurs in leukemia and is here attributed to the nuclein of the broken-down leukocytes. Even sufferers from chronic gout excrete more uric acid when fed with thymus, but the increase is proportionately less than in normal subjects. Nor is the deposition of crystalline uric acid necessarily due to excessive excretion. In leukemia it sometimes results from this cause, but many other factors are concerned, such as the degree of acidity, the proportions of salts and other constituents in solution, and, as Klemperer has shown, the amount of urochrome present. This observer finds that deficiency of urochrome has an important influence in favoring the deposition of uric acid.

Here, again, apart from any excessive excretion of uric acid, there is a

clinical association often observed between the deposition of uric acid sand, the formation of uric acid calculi, and the familiar phenomena of gout. The nature of this association is not yet clearly understood.

In addition to uric acid the urine contains smaller quantities of the closely allied purin bases, xanthin, hypoxanthin, etc. These bases also are partly of exogenous and partly of endogenous origin; being more soluble they play little known part in pathology, but in very rare cases xanthin calculi have been formed in the kidneys or urinary passages.

No idea of the amount of purin substances excreted can be obtained save by exact quantitative estimation of the daily totals. The estimation of uric acid can now be carried out without any special difficulty by Hopkins' method, while the purinometer of Walker Hall allows an estimate of the total purin output, both uric acid and xanthin bases, by a method so simple that it is available for clinical purposes.

In conclusion, it may be mentioned that kidneys damaged by disease appear to exercise a less pronounced retentive effect upon the comparatively insoluble uric acid than upon the very soluble urea.

**Creatinin Excretion.**—Creatinin derived from the creatin of muscle is partly an exogenous and partly an endogenous urinary constituent to the amount of about 1 gram per diem. The exogenous excretion is derived from the meat taken as food. The endogenous excretion, which may be estimated by placing the patient on a creatinin-free diet, has been found to be increased during acute fevers, and, indeed, in any condition which is accompanied by an excessive breaking down of the muscular tissues. In cases with conspicuous splenic enlargement Macleod has found the endogenous creatinin much diminished, and in diseases in which chronic atrophy of muscles is a feature, such as progressive muscular atrophy and the myopathies, a diminished output is also observed, the total bulk of muscle tissue being in such cases much below the normal. The introduction of a new method of estimating creatinin in urine by Folin has led to a considerable increase in our knowledge of the variations in excretion of this substance in different diseases. The method consists in treating 10 cc. of urine with 15 cc. of a saturated solution of picric acid, and 5 cc. of 10 per cent. caustic soda solution, when a deep red color develops. The mixture after standing for five minutes is diluted up to 500 cc. with water, and the solution compared colorimetrically with a standard solution of potassium bichromate. Creatinin in the urine has a direct connection with the closely related chemical substance creatin occurring in the muscular system; but the exact nature of this relation is not definitely settled. Normally the amount of creatinin in the urine is independent of the amount of protein in the food or the total nitrogen in the urine and is a constant quantity for each individual. Creatin does not occur in normal urine, and appears only in minimal quantities after ingestion or subcutaneous injection of this substance. Under pathological conditions a rise in creatinin output is found in maniacal conditions, fever, acromegaly, and exophthalmic goitre. Diminished creatinin excretion is associated with depressed cellular activity as in the muscular dystrophies, lymphatic leukemia, and starvation. The excretion of creatin is distinctly



pathological, and is said to be associated with such conditions as acidosis in diabetes mellitus and cyclical vomiting, and more particularly in malignant disease of the liver. However, Greenwald, and Graham, and Poulton have shown that the presence of aceto-acetic acid in urine introduces serious errors into estimations of creatinin and creatin by the Folin method. It is, therefore, necessary that the question of the excretion of creatin in conditions associated with acetonuric should be investigated afresh. Small quantities of creatin are found during menstruation and throughout pregnancy.

**Phosphaturia.**—The term phosphaturia as commonly applied is a misnomer, seeing that the deposition of amorphous phosphates in the urine is no indication of an abnormally great excretion of phosphoric acid, but merely of the abolition of its normally acid reaction. Such deposition occurs when the urine undergoes ammoniacal decomposition, but these cases are not spoken of as examples of phosphaturia.

Alkalinity from fixed alkalis may be brought about in various ways, and its inevitable result is a separation of the earthy phosphates. Often it is a physiological event, and results from such simple causes as the taking of a diet rich in vegetables, or the drinking of alkaline mineral waters. Again, during the so-called "alkaline tide" which sets in some hours after a meal, the urine may become amphoteric or alkaline, not by the addition of alkali but by the withdrawal of acid in the secretion of the gastric juice. A like result may follow copious vomiting or lavage of the stomach.

The excretion of alkaline urine as the result of none of these causes occurs as a definite pathological event which is often associated with neurasthenic symptoms and is apt to assume in the minds of the patients a gravity out of all proportion to its real importance. In a considerable class of cases such phosphaturia is associated with disorders of the sexual organs. The pathology of many of these cases is very obscure.

In a certain class of case, which is especially common among children, the urinary anomaly is due to an excessive output of calcium in the urine. The excess of calcium combines with the phosphoric acid and causes a relative increase of insoluble basic phosphates and a relative decrease of the soluble acid phosphates to which the acidity of the urine is due.

It is a well-known fact that in health the bulk of the calcium is excreted by way of the colon, and only a relatively small amount in the urine. Soetbeer, who has made a special study of the condition under consideration and whose results have been confirmed by Tobler and other observers, found that in association with the increase of calcium in the urine there is in these cases a diminution of its intestinal excretion. Soetbeer, therefore, places the seat of the morbid process in the mucous membrane of the colon, a species of colitis. It must not be supposed, however, that all cases of phosphaturia in children are of this nature.

In cases of phosphaturia with increase of urinary calcium a regulation of diet, with substitution of food poor in calcium for those rich in salts of that metal, is indicated. In cases with nervous disturbances general tonic treatment usually proves the most useful. The administration

of acids with a view to increasing the urinary acidity is very uncertain in its effects; but R. Hutchison has shown that acid sodium phosphate is more effectual than mineral acids, a result which agrees with what might be expected on theoretical grounds, viz., that an increase of phosphoric acid in the urine would rather tend to manifest itself by an increase of the acidity than by the production of the phenomenon commonly spoken of as phosphaturia.

**Oxaluria.**—From the clinical stand-point, the importance of calcium oxalate as a urinary constituent is due to its sparing solubility and the frequency with which it is deposited in crystalline form, or even appears as concretions in the kidneys or bladder. Such deposition of calcium oxalate depends upon the interaction of a variety of causes of which excessive excretion is only one, although by no means unimportant.

Of the small daily output of oxalic acid in human urine which, under normal conditions, does not exceed 1 or 2 mg., part is exogenous and derived from vegetable foods, and part is endogenous. Even upon an oxalate-free diet, such as pure milk, as also during abstinence from food, some oxalate continues to be excreted. Only a portion of the oxalate of the food finds its way in the urine; some is apparently decomposed in the alimentary canal rather than broken up in the tissues, seeing that injected soluble oxalates are excreted quantitatively. The administration of hydrochloric acid has been shown to promote the absorption of calcium oxalate from the food and to increase the urinary output; and it is probable that in the cases described by Begbie and others as examples of an oxalic acid diathesis, attended with neurasthenic symptoms, the deposition of oxalate crystals in the urine was, as Dunlop suggested, largely due to such increased absorption as the result of the acid dyspepsia which was a prominent phenomenon of the condition.

In the older literature of the subject no clear distinction was drawn between the formation of crystals of calcium oxalate and an actual excessive excretion. Wide variations in daily output undoubtedly occur, some of which are due to the taking of vegetable foods rich in oxalate, such as rhubarb and spinach, as in the cases in which rhubarb freely eaten causes hematuria and the urine deposits crystals of calcium oxalate in great abundance. Increased excretion of oxalic acid has been observed in a variety of diseases, and especially in connection with jaundice and with diabetes; but in no disease is such excessive excretion found to be constant, nor is there any sufficient evidence of the occurrence of a metabolic error as the result of which an increased output of endogenous oxalate, as distinguished from the deposition of crystals, persists over long periods. The origin of the endogenous oxalic acid is still very obscure—some of it is probably of protein origin, some may be derived from purins, and it has been shown by Lommel that the administration of gelatin by the mouth is followed by an increased oxalate excretion; this suggests the gelatin of the tissues as one at least of its probable sources.

In the present state of our knowledge, attempts to combat the tendency to deposit calcium oxalate from the urine may be directed along two separate lines. In the first place we may limit the output by eliminating

as far as possible from the diet articles containing oxalic acid. Many vegetables come into this category, and especially rhubarb, spinach, and tea, and on the basis of Lommel's observation gelatin should also be excluded. In the second place we may seek to produce the conditions best calculated to further the holding of calcium oxalate in solution. The acidity of the urine may be augmented by a meat diet, and following the lines suggested by Klemperer and Tritchler we may endeavor to diminish the calcium of the urine, and at the same time to increase the amount of magnesium present. The authors quoted have shown that whereas excess of calcium salts tends to further precipitation, excess of salts of magnesium tends to inhibit it. This object may be attained by the avoidance of foods rich in calcium, such as milk, eggs, etc., and the prescription of vegetable foods comparatively rich in magnesium, such as rice, farinaceous foods, peas, beans, and coffee.

**Leucin and Tyrosin in Urine.**—The excretion of these amino-acids in the urine was first observed by Frerichs in a case of acute yellow atrophy of the liver, and it is with this disease that their excretion is especially associated and acquires considerable diagnostic importance. In cases of phosphorus poisoning also they are sometimes met with, but much less frequently, and as a rule in smaller quantities.

In cirrhosis of the liver they have been sought for in vain, but Dixon Mann described their presence in the urine in some cases of nutmeg liver resulting from cardiac disease. In pernicious anemia they have occasionally been found. That these protein fractions are sometimes excreted unchanged by cystinurics is undoubted. Tyrosin is occasionally deposited from urines containing it as a sediment of delicate acicular crystals grouped into sheaves, whereas leucin is hardly ever thrown down spontaneously. Usually the crystallization of both substances occurs only after the urine has been concentrated, and when their presence is suspected the urine of twenty-four hours should be precipitated with lead acetate and filtered. After the excess of lead has been removed by a stream of sulphuretted hydrogen, and the lead sulphide filtered off, the filtrate is evaporated down to a syrup. From the residue the bulk of the urea may be removed by treatment with cold absolute alcohol, and what remains is extracted by boiling it with dilute ammoniacal alcohol. The filtered extract is once more evaporated to a small bulk and allowed to stand. Needles of tyrosin and greenish spherules of leucin may then be deposited. Care must be taken not to mistake spherules of ammonium urate for leucin.

To insure certainty special tests for leucin and tyrosin should be employed, and Millon's test should at any rate be tried. All urines yield some pink color when heated with Millon's reagent, even in the cold. When much tyrosin is present the reaction is very intense on warming. When the urine gives no more coloration than does a control of normal urine the presence of any considerable quantity of tyrosin may be excluded.

Since Jacoby showed that in aseptic autolysis of the liver leucin and tyrosin are abundantly formed by the action of the enzymes upon the proteins of the organ, the view has gained acceptance that their excretion



is a result of an autolysis *intra vitam*, and receives support from the fact that in acute yellow atrophy these amino-acids are present in quantity in the liver, as well as in the blood and urine. On the other hand, Neuberg and Richter suggest that the destruction of the hepatic parenchyma, which certainly occurs, does not suffice as the source of the amounts of leucin and tyrosin sometimes found in the blood.

It seems probable that the occasional excretion of leucin and tyrosin in cystinuria is due to a wholly different cause from that in liver disease, and is part of a widespread failure to deal with protein fractions.

**Alkaptonuria.**—This is a very rare urinary anomaly, of which some 40 or 50 cases are on record. Alkapton urine darkens on exposure to air, passing through shades of brown to absolute blackness. The darkening, which is accompanied by absorption of oxygen, is greatly hastened by the addition of an alkali. When the urine is heated with Fehling's solution, a deep brown color develops and a copious reduction occurs. An ammoniacal solution of silver nitrate is quickly reduced by it in the cold. When it is heated with Nylander's solution a darkening occurs, due to the action of the alkaline reagent upon the urine, but no black precipitate forms from reduction of bismuth salt. When a *dilute* solution of ferric chloride is added to the urine drop by drop a deep blue color appears for a moment as each drop falls, until oxidation is complete.

The condition is usually detected during infancy by the staining of napkins as by photographic reagents, or in later life in consequence of the reducing action. In later life alkaptonuria individuals may have osteo-arthritic changes and show staining of cartilages and other tissues known as ochronosis.

Alkaptonuria is not a disease but rather a "sport" of metabolism or chemical malformation. It is congenital, lifelong, and harmless, and apt to occur in families, not a few of whom are the offspring of consanguineous marriages. It is rarely directly inherited. The error consists in a failure to complete the katabolism of the aromatic fractions of proteins, tyrosin and phenylalanin, and the peculiar properties of the urine are due to the presence in it of an aromatic acid derived from these, homogentisic or hydroquinone-acetic acid. The statement that a second aromatic acid, uroleucic, is also present in some cases rests upon a misapprehension.

**Cystinuria.**—The excretion of cystin in the urine is of considerable clinical importance, because this sparingly soluble substance is readily deposited, and cystinurics are very liable to develop renal or vesical calculi and to suffer from cystitis. The condition, which is rather less rare than alkaptonuria, is recognized by the formation of a sediment of very characteristic colorless hexagonal crystals, soluble in ammonia and in hydrochloric acid. Faintly tinted crystals of uric acid sometimes assume a somewhat similar shape, and starch granules and crystals of iodoform have been mistaken for those of cystin. If some of the sediment be dried upon a slide and some strong hydrochloric acid be allowed to flow over the crystals beneath a cover-glass, while the changes are watched through the microscope, beautiful prismatic crystals of cystin-hydrochlorate are seen to grow out rapidly from each hexagonal crystal, and

to form a rosette which melts away as rapidly as it was formed on the addition of a drop of water.

It was shown by Baumann and Udranszky that some cystinurics excreted the diamines cadaverin and putrescin in their urine and feces, and their observation has been repeatedly verified. However, in a number of recent cases they have not been found, and in others they have only been present at intervals, on isolated days or on several successive days. In the feces they have been comparatively seldom found. Cadaverin is much more frequently present than putrescin, but the two may occur in association. Still more rarely leucin and tyrosin have been found.

### PROTEINS IN URINE OTHER THAN NORMAL SERUM PROTEINS

When a protein foreign to the blood plasma is present in it, in any but very small quantities, it is got rid of by excretion by the kidneys. Hence the presence of such proteins in the urine has a wholly different significance from albuminuria, and in no way implies damage to the kidney. Small quantities of foreign proteins, on the other hand, may continue to circulate in the blood until disposed of in other ways.

**Hemoglobinuria.**—When hemolysis of moderate degree is in progress, as in pernicious anemia, the liberated blood pigment becomes converted into bile pigment, and the only effect upon the pigmentation of the urine is due to the presence of excess of urobilin, formed by the action upon the bilirubin of intestinal bacteria. When, however, a great and rapid hemolysis occurs from any cause unchanged blood pigment is excreted by the kidneys and hemoglobinuria results. Hemolysis of the necessary degree may be brought about by a variety of different causes. It is a well-recognized fact that transfusion of foreign blood, *i. e.*, of the blood of an animal of different species, is followed by hemoglobinuria, and one may suppose that the corpuscles which are broken down are those of the foreign blood. A number of poisons exert powerful hemolytic actions, and of these potassium chlorate is the most important. Arseniuretted hydrogen and toluene-diamine also call for mention.

Bacterial poisons of various kinds have like effects, as witness the hemoglobinuria which sometimes occurs in fevers. To this group probably belongs the hemoglobinuria of new-born children which was first described by Winckler. The hemolytic action of malarial parasites is well known, and in the variety of malaria known as black-water fever hemoglobinuria is a prominent symptom. Hemoglobinuria may also follow extensive burns, and is sometimes seen in athletes and others after violent muscular exertion.

The most remarkable of all the varieties is that known as paroxysmal hemoglobinuria, the pathology of which is still very obscure. In some cases this malady would appear to have a syphilitic origin and in others a malarial, but not unfrequently no such antecedent cause can be traced. The exciting cause of the individual paroxysm is, in the great majority of cases, exposure to cold, and this connection is so obvious that it may

be predicted with certainty that an adequate exposure will precipitate an attack. In a few other cases muscular exertion or traumatism figures as the exciting cause.

In association with a paroxysm of hemoglobinuria some of the symptoms of peripheral asphyxia are almost invariably present, and in some cases the symptoms of Raynaud's disease are very pronounced. However, the association is a somewhat one-sided one, for in the majority of cases of Raynaud's disease, even of an extreme degree, hemoglobinuria does not occur. The symptoms develop shortly after the exciting exposure to cold, and after persisting for a few hours gradually pass away, leaving the patient apparently well until the next exposure. In some cases anti-syphilitic treatment has appeared to work a cure, and in some quinine has been found beneficial.

In appearance the urine of hemoglobinuria varies greatly. In the slighter degrees, such as are sometimes met with in fevers, it may be pink and transparent, and may show the spectroscopic bands of oxyhemoglobin with great distinctness. In cases of poisoning by potassium chlorate the pigment set free is wholly or almost wholly in the form of methemoglobin. In paroxysmal hemoglobinuria the urine has a deep red or brown color approaching to blackness, and usually deposits a sediment of hemoglobin debris of a chocolate color. On spectroscopic examination the absorption band, in the red, of methemoglobin is usually clearly seen, as well as the bands of oxyhemoglobin.

In all cases the diagnostic feature of hemoglobinuria, as distinguished from hematuria, is the absence of red corpuscles in the sediment. The particles of brownish debris are often seen to be grouped into cast-like forms. The presence of methemoglobin in the urine is in no way peculiar to hemoglobinuria, for the smoky urine of hematuria also contains the blood pigment in this form. In paroxysmal hemoglobinuria some albumin may persist in the urine for a time after the blood pigment has ceased to be excreted.

**The Bence-Jones Protein.**—The excretion of this peculiar protein substance, which was first described by Bence-Jones in 1848, is one of the most remarkable of urinary anomalies. It is an albuminous substance which is not known to be formed in the organism under normal conditions; and as a constituent foreign to the blood it is readily excreted even by intact kidneys and often in large quantities, up to as much as 70 grams in the twenty-four hours. Although rare, the phenomenon is of great diagnostic importance, seeing that it may be the earliest recognized sign of an affection of the bone marrow known as multiple myeloma.

The recognition of the substance presents no great difficulty when once its properties are known. It is distinguished from the ordinary proteins of albuminuria by its very low temperature of coagulation. The urine begins to show turbidity when warmed to 50° C., or even below that point, and between 50° and 60° C. a bulky flocculent precipitate appears which clings with great tenacity to the sides of the test tube and rises up in the froth which is abundantly formed. Further heating, especially after a few drops of acetic acid have been added, causes the precipitate to be redissolved, but some turbidity usually



persists. The degree of clearing which occurs as the boiling-point is approached varies and depends, as Magnus Levy has shown, rather upon the presence of other substances in solution than upon any inherent property of the protein itself. On cooling, the precipitate reappears, and by alternately heating and cooling the urine precipitation and re-solution may be indefinitely repeated. When the hot test tube is plunged into cold water the appearance of the precipitate showering down through the cooling liquid is very striking and characteristic. If the cold nitric acid test be alone employed the substance may easily be mistaken for albumin, as a similar white ring is formed. With salicyl-sulphonic acid, picric acid, and other reagents employed for the detecting of proteins, precipitates are formed which disappear more or less completely on heating. With hydrochloric acid a dense precipitate is obtained.

**Albumosuria and Peptonuria.**—Some confusion surrounds the use of the terms albumosuria and peptonuria. Whereas some confine the name albumosuria to the excretion of the Bence-Jones substance, which, as we have seen, is not really an albumose, and speak of the excretion of proto- and deuto-albumoses as peptonuria, others, employing the name peptone in Kuhne's more restricted sense as a designation for the only protein which is not precipitated by saturation of its solutions with ammonium sulphate, speak of the excretion of proto- and deuto-albumoses as albumosuria. It is only recently that Kuhne's peptone has been found in the urine by Ito.

Although the excretion of proto- and deuto-albumoses is by no means rare it is not a conspicuous phenomenon from the clinical standpoint, and the quantities excreted are in no way comparable with those of the Bence-Jones protein found in cases of multiple myeloma. Moreover, the characteristic reactions are frequently masked by the simultaneous presence of albumin. Only comparatively rarely is a considerable quantity of albumose recognizable by the ordinary albumin tests.

The albumoses are not precipitated by heating after the addition of a few drops of acetic acid. Many albumin test reagents precipitate them, and the precipitates formed are cleared by heating. The addition of nitric acid in the cold, of picric acid, and of potassium ferrocyanide and acetic acid produces precipitates which behave in this manner. When nitric acid is used error may arise by the formation, in a concentrated urine, of a colorless precipitate of uric acid which is dissolved on heating and forms again on cooling; but any doubt may be cleared up by diluting the urine before the test is applied.

Salicyl-sulphonic acid is a very satisfactory reagent for the detection of albumoses in the absence of albumin. The precipitate which forms when a few drops of a saturated solution of the acid are added to the urine in the cold is soluble on heating. The reaction is a very delicate one and this reagent only precipitates proteins. For the detection of small quantities of albumoses in the presence of albumin Devoto's method is perhaps the simplest. It is based upon the fact that when urine is saturated with ammonium sulphate, albumin and albumoses are alike precipitated. If, however, the saturated urine be boiled, the precipitate of albumin is thereby rendered insoluble in water, whereas

that of an albumose is still soluble. The precipitate filtered off after boiling is therefore washed with water, and to the washings the tests for albumoses are applied.

The biuret reaction is often recommended for the detection of albumoses in urine, and may be conveniently applied as a ring test by gently pouring the urine upon the surface of a layer of cold Fehling's solution. If an albumose be present a pink ring will appear at the junction of the liquids, whereas an albumin yields a violet-colored ring. However, as Stockvis showed, this test is not reliable when it is applied to urine, since urobilin yields a similar pink tint. If the test be used care should at least be taken to exclude, by a preliminary spectroscopic examination, the presence of any considerable quantity of urobilin.

Albumosuria is met with when considerable quantities of protein material are undergoing autolysis *intra vitam*, as, for example, in cases of acute yellow atrophy of the liver and of phosphorus poisoning and during the absorption of pneumonic exudates. During the rapid involution of the uterus after parturition a physiological albumosuria occurs. The albumosuria of fevers, which is usually slight in degree, may be ascribed to the increased protein breakdown which accompanies the febrile state, and that which accompanies extensive ulcerative lesions of the intestine is usually set down to the permeation of the ulcerated surfaces by albumoses from the alimentary canal.

True peptone was found in the urine by Ito, in association with other proteins, in cases of pneumonia and of tuberculous disease of the lungs. Nucleohiston has been found in the urine of patients suffering from pneumonia and from some other febrile maladies, and also in a case of lymphatic leukemia.

**Sugars in Urine.**—The excretion of a sugar in the urine, even in quantity sufficient to yield the ordinary reduction tests, is not necessarily a morbid event. Any healthy individual will excrete glucose provided that a sufficient quantity be taken, in one dose, by the mouth. The quantity usually required to bring about this result is from 150 to 200 grams, and in various morbid conditions the power of dealing with glucose is conspicuously lowered. Such alimentary *glycosuria ex saccharo* requires to be carefully distinguished from that which results from the free eating of starchy foods, *glycosuria ex amylo*, which is always a morbid event and represents the slightest degree of diabetes mellitus.

In young infants who are upon an exclusive milk diet, alimentary lactosuria is not uncommon, and a five-carbon sugar appears in the urine when as much as a liter of a fruit syrup is taken, the power of dealing with sugars of this class being comparatively small. Apart from such conditions and the excretion of lactose by nursing women, the excretion of quantities of sugar readily appreciable by the tests in ordinary use must be classed as a sign of disease.

**Glucose.**—The question of the causation and significance of glycosuria is intimately associated with the study of diabetes, and has been fully discussed under that head.

**Levulose.**—After a sufficient dose has been taken by the mouth, levulose appears in the urine just as glucose does under like conditions.

However, the katabolism of levulose in the organism appears to follow a different path than that in which glucose is dealt with, and alimentary levulosuria has acquired a greatly enhanced clinical interest by the observations of H. Strauss and others, who have shown that the power of destroying this sugar is conspicuously impaired in various forms of hepatic disease. In this way a valuable test of the functional integrity of the liver is afforded.

It is a recognized fact that many diabetic subjects can utilize levulose far better than glucose, but the excretion of greater or less quantities of levulose in association with dextrose appears not to be uncommon in diabetes, and the amount of levulose is in rare instances nearly as great as that of dextrose. In such cases administration of levulose by the mouth has not increased the output of levorotatory sugar, and in a case of mixed mellituria, investigated by Otto Neubauer, glucose given by mouth was excreted in part as such, and in part as levulose.

To a quite different class belong the very rare cases in which levulose is excreted alone in the urine, one of which was most thoroughly studied by Otto Neubauer, who recovered the sugar in crystalline form. A diet free from carbohydrates caused disappearance of the sugar from the urine, but tolerance for starch, and even for glucose, was in no way diminished. Even inulin, which stands to levulose in the same relation as starch does to glucose, caused no obvious increase of the output, which was wholly determined by the presence in the food of levulose as such, or in combination with glucose as cane sugar. Any administration of levulose was followed by its appearance in the urine, but whatever the quantity taken, from as little as 3.8 to as much as 50 grams, approximately the same fraction of the total, about 15 to 17 per cent., appeared in the urine unaltered.

**Lactose.**—The excretion of lactose during lactation is a familiar event and attains its maximum when for any reason nursing is suddenly arrested. Again, as has already been mentioned, alimentary lactosuria is not uncommon in young infants. Lactosuria has no pathological significance, but is one of those harmless conditions which require to be borne in mind lest a wrong interpretation be put upon them. Lactose, maltose, and isomaltose have also been detected in urine, but their presence has no clinical importance so far as known.

**Pentoses.**—The sugars which contain five carbon atoms in chain, instead of six, are abundantly present in plants, but it is only in recent years that members of the group have been recognized as constituents of animal tissues and rarely in the urine. Pentoses in considerable amounts may be introduced into the alimentary canal in vegetable foods, and as the power of the organism to destroy such sugars is much less than in the case of the members of the hexose group, they not infrequently are excreted in appreciable quantities after the free eating of certain fruits, such as plums and cherries, when beer is freely used, or when quantities of prepared fruit juices are taken. Again, in some cases of diabetes traces of pentose have been detected in the urine, but the nature of the pentose present has not yet been determined.

In certain rare cases the excretion of a pentose, racemic arabinose, to



the amount of several grams per diem persists year in and year out, and perhaps throughout life, without any detriment to health.

It is probable that pentosuria, which is a rare anomaly and apparently a harmless one occurring in families many of whom are of the Jewish race, should be classed with such sports of metabolism as alkaptonuria and cystinuria. Its clinical importance lies in the fact that those who exhibit the anomaly are usually looked upon as diabetics; dietary restrictions are in these cases unnecessary and not called for.

**Glycuronic Acid.**—Although not a sugar, glycuronic acid has such intimate chemical relationships with the members both of the hexose and pentose groups that it calls for mention among the reducing substances which are met with in urine. It is excreted in combination with a variety of ingested substances, such excretion being the outcome of a protective mechanism by which the substances in question are rendered harmless and escorted out of the body. Thus the presence of a compound glycuronic acid is no more a pathological event than that of hippuric acid, in which glycocholl fulfils a similar function, and its explanation is to be sought in the excretion of the substance combined, rather than in any disturbance of metabolism. Whether or not glycuronic acid is a normal intermediate product in the katabolism of glucose is still an open question. It is derived from glucose by the oxidation of the alcohol grouping in the molecule, whereas the aldehyde grouping, to which the reducing power is due, remains unaffected. Emil Fischer is inclined to think that the noxious substance is primarily combined with glucose, and that the oxidation to glycuronic acid is effected later.

Although the acid itself is dextrorotatory, the compound glycuronates met with in urine are levorotatory. They differ greatly in their stability; some, such as menthol glycuronic acid, undergo spontaneous decomposition in urine. Among substances the administration of which leads to the excretion of considerable amounts of the conjugated glycuronates are chloral, morphine, camphor, and copaiba, but even apart from drugs and foods the protective mechanism is called into play, and traces of indoxyl glycuronate, and perhaps others, are met with in normal urine.

**Recognition of Sugars in Urine.**—The ordinary chemical tests merely afford evidence of the presence in the urine of a reducing substance which may or may not be a sugar. It is only by the employment of further methods that certainty upon the point may be obtained, and that the particular kind of sugar can be determined.

In actual practice, if a conspicuous reduction occurs when hot Fehling's solution is added to hot urine, neither liquid actually boiling, there is little chance of error in making the diagnosis of glycosuria. When reduction is only obtained after boiling the mixture for some time, or when it is cooling, the evidence is not conclusive, especially if a pea-green opacity alone develops. Such a reaction may be, and often is, due to the presence of a small quantity of glucose, but it may also result from other causes, and confirmatory tests are necessary. In concentrated urine slight reduction may be brought about by uric acid and creatinin, or by salicyluric acid, when salicylates are taken as drugs. Sugars other than glucose may give rise to error and of these lactose is the commonest

With lactose the reduction is less prompt than with glucose, and does not occur below the boiling-point.

Levulose cannot be distinguished from glucose by the copper tests. There is a consensus of opinion that in cases of pentosuria the reduction is usually delayed, and is apt to occur suddenly during cooling. However, Bial denies that this is a characteristic of fresh pentose urines, and has seen the reduction occur before the boiling-point is reached. As a rule, in pentosuria the reaction is as that yielded by 0.5 per cent. of glucose.

The compound glycuronates reduce copper, but not all with equal readiness. Homogentisic acid reduces Fehling's solution readily, but to anyone familiar with alkaptonuria the darkening of the liquid when heated with the alkaline reagent, a change which precedes the reduction of the copper salt, at once suggests the true diagnosis. In carboluria a slight reduction occurs after boiling for some time, and is attributed to hydroquinone, which is excreted in combination with sulphuric acid, by which combination its characteristic reactions are masked.

The *polarimeter* affords important information as to the presence and nature of sugars in urine. A strong dextrorotatory effect is highly suggestive of glucose, but lactose is also dextrorotatory. Levulose is, of course, levorotatory, and when present in association with glucose it counteracts to some extent, and may even completely balance, the dextrorotation due to the latter sugar. This fact renders the quantitative estimation of glucose in urine by means of the polarimeter uncertain, and may explain discrepancies between the results so obtained and those of the reduction methods. In a similar manner the rotatory effect of glucose may be partly masked by the presence in abundance of the levorotatory  $\beta$ -oxybutyric acid, which plays so important a part in the causation of diabetic coma.

The only sugar met with in urine which is actually optically inactive is the racemic arabinose of true pentosuria. The urine is also optically inactive in alkaptonuria. Glycuronic acid is dextrorotatory, but the compound glycuronates which are met with in urine have a levorotatory action. By boiling the urine with hydrochloric acid the compound glycuronates are broken up and the original levorotation is replaced by the dextrorotation of the freed glycuronic acid.

To sum up, dextrorotation by a urine which contains a reducing substance indicates the presence of glucose, unless the conditions are such that lactosuria may be present. Levorotation may be due to levulose, or to compound glycuronates. If the urine be optically inactive there may be balancing quantities of glucose and levulose, or the sugar may be a pentose, or the reducing substance may not be a sugar at all.

Further and most important information is supplied by the fermentation test. Whereas glucose and levulose are readily fermented by yeast, lactose, being a disaccharid, is not fermented until it has been split into dextrose and galactose, and no fermentation occurs within the twenty-four hours usually allowed for the test. The pentoses do not undergo fermentation, and the compound glycuronates also resist the action of yeast. In performing the test it should be remembered that the action of yeast is inhibited by exposure to too high a temperature.

A further means of discrimination is thus afforded. A levorotatory reducing substance which is removed by fermentation is presumably levulose, as the compound glycuronates are not destroyed by yeast. If a dextrorotatory urine becomes levorotatory after fermentation, the levorotation is probably due to  $\beta$ -oxybutyric acid, the glucose having been destroyed. If the reducing power is absent after fermentation from a urine which was originally optically inactive, a balanced admixture of dextrose and levulose may be suspected. A dextrorotatory sugar which does not ferment is presumably lactose, and when dextrose and pentose are present in association the former will be destroyed by fermentation, and the urine which still retains the reducing power of the pentose will now be optically inactive.

A reducing substance which is optically inactive and does not ferment may be pentose (racemic arabinose) or some of the reducing substances which are not sugars, of which the most potent is homogentisic acid.

The phenylhydrazine test also supplies valuable indications which help in the differentiation of sugars. When a crystalline product is obtained it is practically significant of the presence of a sugar. It is true that glycuronic acid forms such a compound, but the conjugated glycuronates do not. However, some of the compound glycuronates, such as that of menthol, are very easily decomposed, and the possibility that the crystals obtained are formed by the liberated glycuronic acid cannot be wholly excluded. A few osazone crystals are not of great significance owing to the extreme delicacy of the test, which is capable of detecting traces of sugar within physiological limits. If the osazone obtained be purified by recrystallization, and its melting-point determined, this affords important information as to the sugar present.

Dextrose and levulose yield the same osazone which melts at  $205^{\circ}$  C. Lactose forms an osazone which melts at  $200^{\circ}$ , but owing to its greater solubility and the small amount of lactose which is usually present in urine, no crystalline product is usually obtained when the test is applied in cases of lactosuria.

Pentosazones, which are easily obtained, may be recognized by their much lower melting-point, between  $150^{\circ}$  and  $160^{\circ}$  C., and the final diagnosis of pentosuria should not be made until a crystalline product of such a melting-point has been obtained.

For the discrimination of special sugars certain substituted phenylhydrazines are of value. Thus, Neuberg obtained, by the use of methylphenylhydrazine, a compound with levulose which melted at  $153^{\circ}$  C., and the same observer has shown that, with parabromphenylhydrazine, glycuronic acid yields a crystalline compound which melts at  $236^{\circ}$  C.

Special tests for certain sugars are also of value. Pentose and also glycuronic acid yield furfural reactions. For the detection of pentoses Bial's modification of the orcin test is especially useful. The reagent is prepared by dissolving 1 gram of orcin in 500 cc. of hydrochloric acid of a specific gravity of 1.151; 20 to 30 drops of a 10 per cent. solution of ferric chloride are afterward added. The reagent should be kept in an amber glass bottle. In testing, 5 cc. of the reagent are heated to boiling in a test tube; after the tube has been removed from the flame, and



boiling has ceased, five drops of the urine to be tested are added from a pipette. If pentose is present a rich green color appears at the junction of the urine and reagent and spreads through the liquid when it is shaken. On examining with the spectroscope a dark absorption band is seen between the solar C and D lines. A second band which is usually seen in the extreme red has no diagnostic importance. It is claimed for this test that when performed in the above manner it is yielded by no urines save those which contain pentose, and the writer's experience confirms this. If, however, the urine and reagent be boiled together, the green color and the characteristic absorption band appear if the urine contains a compound glycuronate. Exact care in preparation of the reagent is necessary, and its efficiency should be tested with a solution of a pentose or with a pentose urine if such be available.

Further evidence is afforded by the phloroglucin test, which is also yielded by glycuronic acid, and confirmation is obtained by preparing a crystalline osazone which, after recrystallization, melts at  $150^{\circ}$  to  $160^{\circ}$  C.

For the recognition of lactose Rubner's test may be employed. The urine is boiled for several minutes with an excess of neutral lead acetate; on addition of ammonia a red color develops and a cherry-red precipitate falls.

Levulose differs from other sugars in yielding Seliwanoff's reaction. The test is carried out as follows: 10 cc. of urine are warmed with a little resorcin and 2 cc. of dilute hydrochloric acid. If levulose be present the liquid assumes a red color and deposits a precipitate which is soluble in alcohol, forming a rich red solution.

**Substances of the Acetone Group.**—The substances grouped together under this name which appear in the urine,  $\beta$ -oxybutyric acid, acetoacetic acid, and acetone, are closely related and form a natural series.

The most important cause of the formation of the acetone substances is apparently the withdrawal of carbohydrates from the food, or inability to burn carbohydrates, as in diabetes. Thus starvation or a carbohydrate-free diet excites acetonuria even in normal individuals, and in the cases of persistent vomiting in which it is a prominent symptom the acetonuria may be due to this same cause. In a variety of morbid conditions in which there is an abnormal tissue breakdown acetonuria is met with, such as fever, carcinoma, phosphorus poisoning; and cyclic vomiting, pernicious vomiting in pregnancy and delayed chloroform poisoning must be included among the conditions in which acetonuria plays an important part. In delayed chloroform poisoning, and also in fatal cases in children in which vomiting is almost the only other symptom save acidosis, advanced fatty changes have been met with in the liver by Guthrie, Langmead, and others. Speaking generally, acetonuria appears to be more easily induced in children than in adults, and is not uncommon in association with bronchopneumonia.

It used to be held that the parent substances of the acetone group are the proteins of the body, but the investigations of Magnus Levy, who showed that the protein breakdown was quite unequal to explaining the enormous quantities of  $\beta$ -oxybutyric acid sometimes excreted in

the urine, and that the excretion of this acid in no way runs parallel with the total nitrogen output, proved that some other source must be looked for, namely, the fats. This has been confirmed by the demonstration that a diet rich in fats causes an increased acetonuria, especially if the fatty acids present are oleic or other lower members of the fatty acid series.

Still more recently the experiments of Embden and others on the production of acetone from certain amino-acids, leucin, tyrosin, and phenylalanin, when these were perfused through the liver, seem to indicate clearly that since acetone is formed from these protein fractions, the proteins of the food and tissues must be looked upon as contributing to the total yield of the substances of the acetone group.

The most important member of the group,  $\beta$ -oxybutyric acid, is the least easy of detection. A rough idea of the amount present may be obtained from the degree of levorotation which the urine exhibits after fermentation with yeast, but in order to obtain any accurate notion of the quantity present, it is necessary to extract the acid by methods which can hardly be classed as clinical; or to convert it into  $\alpha$ -crotonic acid and to estimate it as such. Again, estimations of the urinary ammonia afford a rough indication of the amounts of  $\beta$ -oxybutyric and aceto-acetic acids which are being excreted in combination with it.

The presence of aceto-acetic acid is indicated by the well-known iron reaction, namely, the development of a deep red-brown color on the addition of a solution of ferric chloride. This test serves to indicate an increase of the substances of the group, and the presence of a higher member of the series than acetone. It therefore affords a very valuable indication that the morbid processes which result in the formation of these substances are actively at work. When patients are taking a salicylate or aspirin this reaction is, of course, masked by the iron reaction due to the drug. When doubt arises whether the color obtained is due to aceto-acetic acid, it may be dispelled by boiling the urine for a few minutes and repeating the test after it has cooled. As a result of such treatment aceto-acetic acid will be broken up into acetone and carbon dioxide and the reaction will no longer be obtained. Acetone as such is present in very small amounts in urine, and the tests supposed to detect its presence, such as that of Rothera, are in reality tests for aceto-acetic acid. In Rothera's test 5 cc. of urine are saturated with ammonium sulphate, 2 cc. of ammonia solution are added, and a few drops of a solution of sodium nitroprusside. If aceto-acetic acid be present a rich purple color gradually develops.

**Lipuria.**—The excretion of fat in the urine in quantities which are appreciable to the eye is a decidedly uncommon symptom. In forms of renal disease in which the kidneys undergo a so-called fatty degeneration, such as chronic parenchymatous nephritis, the microscope shows fat globules in shed epithelial cells and in casts, and even free globules or crystals of fat may be present. In chyluria the milky appearance of the urine is due to the presence of minute fat particles. In cases in which malignant growths of the kidneys were breaking down larger quantities of fat have occasionally been detected in the urine. Apart

from these local forms of lipuria, there are others in which lipuria is an outward sign of lipemia, and in any condition in which there is an accumulation of fat in the blood it may find its way into the urine.

The administration of large quantities of fat by the mouth may give rise to lipuria. During pregnancy the excretion of fat has been observed and a lipuria of moderate degree may be met with in cases of diabetes mellitus, phthisis, and other conditions attended by rapid wasting, acute yellow atrophy of the liver, and phosphorus poisoning. Fractures of long bones and the operation of osteotomy may be followed by the escape of fat into the blood, as is witnessed by the phenomenon of fat embolism, and may give rise to a considerable lipuria.

In any case in which the urine is found to contain fat it is important to exclude accidental or intentional admixture, as by the use of an oiled catheter or the addition of milk to the urine after it has been passed. In true lipuria the fat may form an emulsion, as in chyluria, or may form a cloud suspended in the liquid, or an oily and transparent or an opaque layer upon its surface. By shaking the urine with ether the contained fat may be extracted, leaving the liquid clear and transparent when the layer of ether has separated from it. When a drop of the ethereal extract is allowed to evaporate on filter paper it leaves a translucent greasy mark. The minute globules in the sediment may be recognized with greater certainty by staining with osmic acid.

Calculi composed of fats have, very rarely, been formed in the urinary passages. The suggestion that in such cases the fat has been introduced per urethram in the form of bougies or otherwise is certainly not tenable in all instances, and Horbaczewski's investigations suffice to establish the reality of *urostealiths* beyond all reasonable doubt. The fatty calculi have usually been coated with a layer of earthy phosphates. As to the significance of such calculi and the nature of the morbid processes in which they have their origin we are still completely in the dark. Not more than five or six such calculi are on record.

**Choluria.**—In cases of jaundice the bile pigment very early finds its way into the urine, and its presence therein may be recognized by the appropriate tests and by the color which it imparts. Uric acid crystals deposited from icteric urines have a leathery brown color when viewed in bulk, and under the microscope the individual crystals are seen to be modified both in tint and in form by the included bile pigment.

Gmelin's test is best carried out by allowing the urine to flow gently on to nitric acid in a test-tube. A play of colors is seen at the junction of the liquids, and the whole of the layer of urine often acquires a lasting green tint. It is necessary that the green color of biliverdin should be obtained, as the chromogens of urine may yield pink or purple rings under the same conditions. Maréchal's test is easily carried out and conclusive. Some tincture of iodine is allowed to flow upon the surface of the urine in a test tube, and a green ring colored by biliverdin appears at the junction layer if bile pigment be present.

In some cases the amount of bile pigment is so small that the above tests yield inconclusive results. In such circumstances Huppert's test is of great value. Any required quantity of the urine may be precipitated



by the addition of milk of lime or of barium chloride and hydrate. The precipitate, which carries down with it all the bile pigment present, is collected upon a filter and transferred to a beaker containing alcohol acidified with sulphuric acid. When the beaker is heated upon the water-bath the bile pigment is converted into biliverdin, which imparts to the acidulated alcohol a rich green color.

Any condition which produces jaundice may cause the appearance of bile pigment in the urine, but the choluria may disappear while the skin is still conspicuously bile-stained. In a very few cases which may be classed as clinical curiosities the urine has been deeply bile-stained, although no jaundice existed. In such cases a fistulous communication has existed between the biliary and urinary passages. The bile salts are met with in the urine in jaundice, but far less constantly, usually only in the early days of the attack and in no large quantities.

Pettenkofer's test is not applicable for the detection of the bile acids in urine, owing to the fact that indican and other constituents contribute to the production of a red color which closely simulates the true reaction. For clinical purposes the best test available is based upon the conspicuous lowering of surface tension which results from the presence of bile salts in solution. A finely divided, light powder, such as flowers of sulphur, is scattered upon the surface of the urine. Under ordinary conditions such a powder remains resting upon the surface of the liquid, but if bile salts be present it rapidly sinks to the bottom.

## CHAPTER XIV

### UREMIA

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THE name uremia is used to designate a group of symptoms which usher in the fatal ending in a large proportion of cases of renal disease. The group embraces a large number of morbid manifestations of widely different characters, only a few of which are usually observed in any individual case, and which assume such diverse grouping that two cases which may, without hesitation, be designated uremic, may, in their superficial aspects, show little in common. The boundaries of the symptom-complex are somewhat ill defined, and whereas some authorities would limit the application of the term uremia to functional disturbances which appear to have a toxic origin, others would extend its signification to include a number of anatomical lesions such as ulceration of the stomach and intestines, stomatitis, and pericarditis; while others again regard as minor uremic phenomena the cardiovascular changes which play so conspicuous a part in chronic renal disease.

Impairment of the renal functions, whatever may be its cause, may bring about a condition of uremia, provided always that both kidneys are implicated; but it is one of the most puzzling features of the condition, and one which opposes the chief obstacle to any satisfactory explanation of its pathology, that complete arrest of the excretory functions of the kidneys, although necessarily fatal unless relieved by surgical measures or otherwise, does not result in the more characteristic uremic symptoms. Unilateral renal disease, even though it result in such complete destruction of the affected kidney as follows the permanent occlusion of one ureter by a calculus, does not give rise to uremia, provided always that the remaining kidney adequately performs its functions.

On account of the protean aspects of uremia, an attempt to describe in detail the features of individual attacks entails needless repetitions, and it will, therefore, be more convenient to begin by considering the various manifestations of the uremic state in turn, and to group them according to the several systems—nervous, alimentary, circulatory, and respiratory—to which they are referable.

**Pathology.—The Condition of the Urine.**—In the majority of instances the onset of uremia is preceded by diminished excretion of urine, and if the scanty urine be of low specific gravity the danger of uremia is the more obvious. In some cases the quantity of urine passed is not below the normal, but when this is the case its specific gravity is usually low. Side by side with a fall of specific gravity goes an elevation of the freezing-point, both being dependent upon a decrease of solids in solution.

Albumin is practically always present in the urine of uremic patients but the quantity varies greatly according to the nature of the primary renal lesion. Casts may or may not be present. The output of urea and of the total nitrogen of the urine has been found to be conspicuously diminished during the days preceding an attack, whereas during and immediately after the attack the excretion may be distinctly increased. An increased excretion of ammonia bears witness to some degree of acidosis.

**The Blood.**—In almost all cases uremia is accompanied by a noticeable increase of the molecular concentration of the blood. This is evidenced by a conspicuous depression of the freezing-point of the serum which, under ordinary conditions, is much more constant than that of the urine, and varies but little from  $-0.56^{\circ}\text{C}$ . However, cases have been met with in which the molecular concentration was little marked, suggesting that the accumulation of waste products in bulk is by no means the only factor at work. On the other hand, a greatly increased molecular concentration of the blood may exist apart from the development of any uremic symptoms.

The molecular concentration in the blood is mainly due to an accumulation of the nitrogenous products of the breaking down of proteins, as is shown by the conspicuous increase of residual nitrogen; that is to say, of nitrogen other than that contained in the blood proteins. This has been clearly brought out by the researches of H. Strauss<sup>1</sup> carried out in Senator's clinic. At the same time no increase is apparent of inorganic salts, such as sodium chloride. The same lesson is taught by the more recent researches by physical methods; for the great depression of the freezing-point of the blood, which is almost constant in association with uremia, is not attended by any increase of electrical conductivity such as would be observed if the molecular richness were due to an increase of dissociable molecules, such as those of salts.

Urea is found in considerable quantities in various secretions and excretions of uremic patients such as the gastric juice, intestinal contents, bile, saliva, and sweat, and in some cases the sweat as it evaporates leaves an efflorescence of crystals of urea upon the skin of the patients.

**Theories of Uremia.**—In the earlier days of the study of uremia the symptoms grouped under that name were ascribed by Traube and others to such causes as oedema of the brain or disturbances of the cerebral circulation. Such views have met with little acceptance in recent years, and the characters of the uremic manifestations are so strongly suggestive of a toxic origin that investigators have, for the most part, sought to explain them as the results of the accumulation in the blood of a poison or poisons. The obvious association which exists between uremia and deficient functional activity of the kidneys naturally suggested that the toxic material might be found among the end products of metabolism, which it is the function of the kidneys to excrete; but in spite of the large amount of research which has been expended upon the problem, from the days of Bright and Addison to the present, no

<sup>1</sup> *Die chronische Nierenentzündungen*, Berlin, 1902.



solution yet proposed has met with general acceptance, and the cause still remains unknown.

The very name uremia, which like so many other incorrect designations has become so firmly established that to attempt to replace it would be alike futile and pedantic, is a legacy of the earliest of all the toxic theories, that which ascribed the train of symptoms to poisoning by urea. It was long ago clearly demonstrated that this theory was untenable, seeing that urea is almost devoid of toxic properties, and may be injected into animals in large doses without exciting any conspicuous symptoms. A similar fate befell the well-known theory of Frerichs, who ascribed uremia not to urea itself but to ammonium carbonate formed from it within the organism by the action of a ferment; and Treitz's modification of that theory, according to which the change from urea to ammonium carbonate was brought about in the alimentary canal, for it was shown that an increase of ammonia in the blood is no constant or conspicuous feature of uremia. The theory of creatinemia also failed to win any general acceptance, nor has it been found that any one of the end products of protein katabolism fulfils the necessary requirements.

In view of this failure to identify among the normal excretory products any single toxic agent capable of explaining the symptoms observed not a few physicians have been led to adopt the view that some intermediate product of metabolism may be responsible. Of such carbamic acid has most in its favor, in view of the phenomena observed in animals with an Eck fistula. Others again hold that the manifestations are rather the results of the retention of the excretory products generally than of the specific toxic action of any one of them. However, a great obstacle to the acceptance of this last view is the fact that the more characteristic symptoms are not seen in cases of complete anuria, in which the kidneys excrete no waste products at all.

Among the older theories that of Bouchard, which was based upon the toxic effects which are observed when urine is injected into the circulation of animals, calls for special mention. The fatal effects of such injections, provided that enough urine be employed, are beyond question, and, in the light of more recent investigations, they appear to be largely due to the toxic action of potassium salts. Various organic constituents of urine, such as creatinin and the pigments, have been shown to be incapable of producing the observed toxic effects, at any rate in such quantities as are in the injected urine, whereas much of the toxic power is retained by the inorganic constituents of the ash.

Bouchard found that the urine of patients with uremia was conspicuously less toxic for rabbits than was normal human urine, and this observation supplied the strongest argument which could be adduced for the applicability of the results of toxicity experiments. He attributed the uremic symptoms mainly to organic toxic substances which are constituents of normal urine, but which he identified only by their physiological action, admitting that some portion of the poisonous effects of injected urine was due to potassium salts. Of the toxins, one induced convulsions, another depressed the temperature, another

exerted a narcotic action, and yet another contracted the pupils. Bouchard's urotoxins still remain theoretical substances, and his conclusions have failed to obtain acceptance from more recent investigators.

The unquestioned toxicity of potassium salts formed the basis of the theory of Feltz and Ritter,<sup>1</sup> who attributed uremia to their action. In support of their theory they brought forward a mass of valuable experimental results, which included demonstrations of the inability of various organic constituents of the urine to induce uremic symptoms. This theory has nevertheless shared the fate of so many others, and later investigators have failed to trace any direct relationship between accumulation of potassium salts in the blood and the development of uremia. Nor are the toxic effects of potassium salts at all strictly comparable with the phenomena of that condition.

The failure which has hitherto attended all attempts to explain the phenomena by the toxic action of any one constituent of the urine, or any combination of excretory products, has led a number of more recent investigators to look for an explanation in other directions. Thus a physical theory has been propounded which attributes the effects to the mere accumulation of molecules in the blood, a molecular overcrowding, so to speak, rather than to any specific toxic action of particular molecules. The name of Lindemann is specially connected with this view. It would appear, however, that uremia occasionally develops apart from any excessive molecular concentration, and in cases in which the freezing-point of the blood is conspicuously depressed symptoms of uremia may be wholly absent.

Some investigators have suggested that the kidneys produce an internal secretion which may play an important part in controlling metabolism. Thus Brown-Séquard found that animals succumbed more quickly after removal of the kidneys than after ligature of the ureters. Ascoli, who has confirmed this observation, ascribes the more rapid death to the loss of the internal secretion of the organs, and in support of this theory he adduces experiments in which the injection of the juice of normal kidneys into animals deprived of their kidneys prolonged life to the limit attained in animals with ligatured ureters.

Rose Bradford's well-known experiments upon dogs suggest that the removal of renal substance within certain limits, as, for example, one kidney and part of the other, causes increased output of water and of the end products of protein metabolism such as urea, and that this may be ascribed to the diminution of a controlling influence exerted by the kidneys upon the metabolic processes, with the result that metabolism runs riot. This would naturally lead to an overloading of the blood with waste products beyond the accumulation resulting from mere retention. Moreover, Bradford has found that in cases of obstructive suppression in which the internal renal secretion might be supposed to be still yielded, the accumulation of waste products in the blood was less than in ordinary cases of uremia.

On the other hand, it must be mentioned that Bainbridge and Beddard,

<sup>1</sup> *De l'urémie expérimentale*, Paris, 1881.

repeating Bradford's experiments with cats, did not constantly obtain an increased output of nitrogen, and regard the increase, when it occurs, as due to inanition, and of the same nature as that in starving animals.

Another recent theory advocated by Ascoli<sup>1</sup> and others is that which attributes uremia to nephrolysins. It has been shown that just as when bacteria find their way into the animal organism substances antagonistic to them are produced, so also when cells of a particular organ are injected *sub cutem*, or into the peritoneal cavity, substances antagonistic to the special cells injected are found in the organism. Of such products, which are collectively spoken of as cytolytins, those which are destructive of red-blood corpuscles, the hemolysins, have been most studied, but the nephrolysins have also attracted considerable attention. When broken-up renal substance is injected into animals, substances are found in the serum of the animals so treated which exert a destructive action upon the renal cells of other animals. When injected into a second animal such a serum sets up a nephritis and causes albuminuria, and the serum of the second animal, when injected into a third, has been found to excite a temporary albuminuria.

It has been suggested that the tendency to chronicity in renal diseases is due to the establishment of a vicious circle, and that the nephrolysins formed as a result of the renal lesions aggravate the morbid condition in the kidneys. It has, indeed, been shown that when nephritis is set up in an animal, by chromic acid or otherwise, the serum of the animal contains nephrolysins which are capable of causing nephritis in a second animal, but it has not yet been conclusively proved that the nephrolysins so formed react upon the kidneys of the animal itself. However, it has been stated that injury to one kidney, such as follows ligation of a ureter, tends to excite disease in the second kidney, but clinical experience of cases of unilateral obstruction by calculus does not appear to support this view. Ascoli records experiments which point to the production of antinephrolsins in animals which are protected by the injection of minor doses of nephrolytic sera.

This observer and those who think with him believe that the phenomena of uremia may result from the action of nephrolsins upon the nerve centres. There is evidence to show that the effects of cytolytins are not confined to the special tissues to which they are antagonistic, but may be more widespread. Moreover, Ascoli found that the injection of normal rabbit serum into the subdural space of dogs produced no obvious effects, and even nephrolytic serum was sometimes equally innocuous; however, in some instances such sera excited general tonic and clonic convulsions and deep coma ending in death.

Our knowledge of the nephrolsins, of their effects upon the kidneys of the animals in which they are primarily formed, as distinguished from those of other animals injected with the nephrolytic serum, and above all of the power of nephrolsins in the general circulation to excite the stormy symptoms of uremia, is still too incomplete for any theory in which they play the principal part to command acceptance. As

<sup>1</sup> *Vorlesungen über Uraemie*, Jena, 1903.



Friedrich Müller has demonstrated, the renal diseases in which uremia is most apt to occur in its most pronounced forms are not always those in which the destruction of renal tissue is most extensive, and although in cases of obstructive suppression it may be that death results before the breakdown of renal substance is sufficient to cause the appearance of abundant nephrolyns in the circulation, such an explanation will not apply to the absence of convulsions and coma in cases of anuria from thrombosis of the renal arteries.

Nevertheless, the theory in question calls for careful consideration, since it introduces new factors derived from a fresh field of study, and deals with classes of products which are still "seen through a glass darkly," the very existence of which was not even suspected until within recent years. Meanwhile the cause of uremia remains unknown.

**Symptoms.—Symptoms Referable to the Nervous System.—*Convulsions.***—These, of greater or less severity, are among the commonest and most conspicuous of the symptoms of uremia. They vary in degree from mere twitchings of muscles to fully developed epileptiform attacks. The latter bear a very close resemblance to true epileptic seizures, and present the ordinary sequence of tonic and clonic convulsive movements, followed often by a longer or shorter period of unconsciousness. Only by the antecedent symptoms, or by the evidences of renal disease, may it be possible to distinguish the condition from epilepsy.

The onset may follow upon a period of chronic uremia, with headache, vomiting, and perhaps dimness of vision, of which the convulsion is merely the culmination. On the other hand, the antecedent symptoms may be very slight, such as headache of no severity, with or without nausea; or, again, the convulsions may set in with stormy suddenness in patients who are not conscious of any impairment of health sufficient to lead them to seek for medical advice, as is the case with not a few of the sufferers from granular kidney.

Occasionally some subjective sensation or involuntary movement, such as is included among the recognized auræ of true epilepsy, precedes the convulsive seizure. Not infrequently the convulsions begin locally, as, for example, in the muscles of the face or of one limb, and they are usually more pronounced in half of the body. As in epilepsy an initial tonic stage, during which the embarrassment of respiration may cause pronounced cyanosis and turgidity of veins, following upon a stage of pallor, is succeeded by a clonic stage during which the tongue may be bitten.

During the fit the pulse, which was previously of high tension in the majority of cases, may become small, rapid, and easily compressible; however, it sometimes happens that the tension is maintained throughout. The pupils are usually dilated and active, but they are in some instances contracted. Sir William Gowers states that nystagmus is sometimes observed, and lays special stress upon the implication of the facial muscles in uremic convulsions. The temperature is usually raised during the convulsive period, but this, like every other rule relating to uremia, is by no means absolute, and the record may be conspicuously subnormal. The fit may be followed by a period of somnolence, as in

epilepsy, or consciousness may not be recovered, the patient remaining in a state of coma, or, again, on recovery he may prove to be temporarily blind. The convulsions may follow each other at considerable intervals, or may recur so quickly that the patient's condition may be described as one of *status epilepticus*. Death may occur during a convulsion, and the first convulsion may prove fatal.

*Paralyses*.—That local paralyses, usually of hemiplegic distribution, may occur in uremic conditions, in cases in which no gross cerebral lesions can be found postmortem other than œdema of the brain and its membranes, may be regarded as an established fact. Such paralyses have occasionally followed upon unilateral convulsions, but in some instances their onset has not been preceded by any epileptiform seizure, at any rate of a conspicuous kind. In some cases there has been right hemiplegia with aphasia, and aphasia has also been met with apart from any paralysis of the limbs. Hemianesthesia has occasionally been observed in association with hemiplegia. The duration of the paralytic symptoms varies greatly in different cases.

*Disorders of the Special Senses*.—Sensory disturbances, and especially disorders of vision, are among the most noteworthy and remarkable of the symptoms of uremia. Doubtless, in some instances, impairment of vision is a result of albuminuric retinitis and of optic neuritis, but it is no less certain that complete amaurosis develops in association with uremic symptoms apart from any changes in the fundus of the eye which can be detected with the ophthalmoscope. Moreover, the sudden onset and transient character of the amaurosis is hardly compatible with the presence of an organic lesion.

Actual blindness may be preceded by a period of dimness of vision, or the stage of dimness may be at no time overstepped. Not infrequently the patient emerges from a convulsive attack completely amaurotic and unable to perceive even a bright light, or, again, the blindness may be, at least for a time, an isolated symptom of the uremic state. The loss of vision may last for a few hours or even less, or for a few days. In some, especially in puerperal cases, a more lasting blindness develops, which suggests that permanent damage has resulted from the lesion to which the amaurosis is due. As the sight is restored recovery is not always uniform over the field of vision, and large areas of blindness may persist for a time after other parts have regained their function.

In uremic amaurosis the pupils usually, but not invariably, retain their activity. A central area of blindness for blue and yellow has been observed after recovery from uremic amaurosis, but, as König presents it and as C. Gerhardt<sup>1</sup> has also shown, central blue blindness is sometimes present in cases of granular kidney apart from any characteristic uremic symptoms, usually in association with albuminuric retinitis but also in cases in which there is little amiss detected with the ophthalmoscope. It would seem to be a renal rather than a uremic symptom. The affections of the sense of *hearing* met with in uremia are of several different kinds. Singing in the ears and noises of various kinds are

<sup>1</sup> *München. med. Wchnschr.*, 1900, xlvii, 1.

comparatively common. Partial deafness is less common and complete deafness is decidedly rare. Tinnitus may be accompanied by partial deafness, or impairment of hearing may be present apart from tinnitus. Dieulafoy<sup>1</sup> described severe pain in the ears and face as an occasional accompaniment of impairment of hearing, but in some of the cases which he quotes definite aural lesions were present, such as perforation of the tympanic membrane, or injection along the handle of the malleus.

*Coma, Delirium, and Mania.*—Drowsiness, apathy, and coma are conspicuous. The onset of coma is often gradual in chronic cases. It may be preceded by mental slowness or drowsiness lasting for weeks, and in favorable cases this stage may never be overstepped, restored functional activity of the kidneys being attended by a corresponding improvement of the mental state. On the other hand, it not infrequently happens that a convulsion of sudden onset leaves the patient in a deeply comatose condition.

The unconscious patient may exhibit twitching of the limbs, or convulsive attacks may occur at intervals. The breathing may be stertorous, or may have the peculiar whiffing character upon which Addison laid special stress. Sometimes it assumes the Cheyne-Stokes rhythm. In some cases the cerebral disturbance assumes a more active form, and a muttering delirium may persist for days with incoherence of words and ideas. Delirium, which may be of all degrees of activity up to actual mania, may be an early symptom of uremia, and may replace coma as the sequel of a convulsive attack.

Occasionally the patient exhibits delusions of persecution and endeavors to leave his bed and to escape from his imaginary persecutors. In other instances the mental derangement assumes a melancholic form, in others, again, it has a religious or erotic character, or there may be acute and violent maniacal outbreaks. The duration of such symptoms is very variable and in chronic cases may be for weeks or months.

*Headache and Giddiness.*—Headache is one of the commonest symptoms, and in chronic cases it is often the earliest of all. The headache has no constant character. In distribution it may be frontal, occipital, or general, and it sometimes has the unilateral distribution which is associated with migraine. It may be slight or of great severity. Giddiness, also, is a common early symptom.

*State of the Pupils.*—This varies so greatly in different cases, and even in the same case at different periods, that it is of comparatively slight diagnostic value. In acute attacks the pupils tend to be dilated, but may be of normal size. In chronic uremia myosis is, on the other hand, by no means uncommon. During a period of amaurosis the pupils usually retain their activity.

**Symptoms Referable to the Alimentary Tract.**—Scarcely inferior in clinical importance to the disturbances of the nervous system are those referable to the alimentary canal. These are seldom wholly absent, and in some cases dominate the clinical picture. *Loss of appetite* and *nausea* are usually complained of, and vomiting is a common symptom,

<sup>1</sup> *Gazette Hebdom.*, 1878, xv, 49.



especially in cases of the more chronic kind, in which headache and vomiting usually precede and usher in the more alarming manifestations, and are often the sole evidences of uremia over considerable periods. Violent and persistent *hiccough* is of very evil omen, and usually precedes a fatal ending by a few days only. In some cases such hiccough is the earliest and most conspicuous uremic symptom in chronic renal disease, and perhaps most often in cases of granular kidney. Diarrhœa, although decidedly less common than vomiting, usually appears in the last stages of chronic renal diseases. The stools contain urea and ammonium carbonate, may be watery or rich in mucus, and may contain material resembling frog's spawn. They are sometimes tinged with blood.

The so-called *uremic stomatitis* has been specially studied by Lancereaux, Hirtz,<sup>1</sup> and especially by Barié,<sup>2</sup> who has published a monograph upon the subject. Barié distinguishes two varieties of such stomatitis; an erythemato-pultaceous and an ulcerative. In the first mentioned form there is at first merely injection and some swelling of the buccal mucous membrane; later, the tongue becomes coated with a grayish tenacious coating, of consistence like glue and of a sickly odor, and the gums and mucous membrane of the buccal cavity acquire a similar pultaceous covering. Beneath this coating the mucous membrane is dry and deeply injected, but is not ulcerated. When the sticky coating is removed it soon reforms. The saliva becomes scanty and tenacious, appetite is lost, and there is a loathing of food. Vomiting usually occurs and sometimes diarrhœa also.

In the second or ulcerative variety, which is far less common, the symptoms at first resemble those of the pultaceous stomatitis, but after a few days ulcers develop upon the gums and buccal surface of the lip, and cheeks. In the centre of the ulcer there is often a caseous patch surrounded by a deeply injected zone. With the development of the ulcers the saliva, which has previously been scanty and tenacious, becomes very abundant and may amount to as much as 800 to 900 cc. in the twenty-four hours. In either form of stomatitis there may be a subjective sensation of heat in the mouth, but this is specially prominent in the ulcerative cases.

*Hemorrhagic erosions* of the stomach have been described by Pineau and by Lancereaux. *Ulceration of the intestines*, although rare, has been met with in a sufficient number of cases to justify its inclusion among uremic, or perhaps to speak more accurately, among renal accidents. The colon, cecum, and lower portion of the ileum are the usual seats of such ulceration.

**Symptoms Referable to the Circulatory System.**—It is probable that the cardiovascular changes which constitute so prominent a feature in chronic renal diseases have their origin in the presence of noxious materials in the circulating blood, and are themselves, in a sense, of uremic origin. There need be little hesitation in asserting that high arterial tension is a natural outcome of uremic poisoning. On the other hand, it is equally certain that high pulse tension is no constant feature

<sup>1</sup> *Semaine Med.*, 1902, xxii, 109.

<sup>2</sup> *Archiv. gén. de Méd.*, 1889, clxiv, 415, 690.

of the condition, and may be wholly wanting in the uremic state. The wide differences observed in the degree of arterial tension in undoubted cases are apparently due to the conflict of two factors, and it would seem that, in addition to the influence of the loaded condition of the blood in raising arterial tension, the enfeeblement of the heart, which is so often present, has a contrary influence which needs to be taken into account. Accordingly, as one or other of these factors predominate, so will the tension of the pulse be high, low, or intermediate in degree. If this be the true explanation of the clinical findings, it will be obvious that, given a condition of uremia, the absence of conspicuously high tension must be looked upon as a by no means favorable sign.

The occurrence of *cardiac failure* in cases of renal disease is a sufficiently common phenomenon, and, in addition to the mechanical strain to which the heart is subjected in its endeavor to overcome peripheral obstruction, degeneration of its muscular walls plays no unimportant part in bringing about such failure. Indeed, experience in the post-mortem room teaches that a large proportion of sudden deaths among persons over forty years of age are due to myocardial degeneration in association with granular kidneys. The rate of the *pulse* also exhibits marked differences. Before the attack, and even during it, the pulse may be slow and irregular, but during the convulsive seizures it is more commonly small, soft, and rapid.

The occurrence of *pericarditis* as a terminal symptom in renal cases, and especially in cases of granular kidney, has long been known and was observed by Bright. Such pericarditis is usually revealed by the development of a loud friction sound, but, as it is generally unaccompanied by any precordial pain or by other symptoms which direct attention to the heart, it may easily be overlooked.

**Symptoms Referable to the Respiratory System.**—*Dyspnœa* is a common symptom, but a study of the cases in which it is present shows that it may arise from several distinct causes. Often the respiratory disturbance is rather to be classed as renal or cardiac than uremic, and in chronic renal diseases there are several factors at work.

The dyspnœa may be of pulmonary origin and due to emphysema, which is, in some degree, an almost constant concomitant of granular kidneys, and is occasionally so pronounced as to dominate the clinical picture. In other cases the dyspnœa is due to a complicating bronchitis, and in others, again, results from cardiac failure, as is evidenced by the state of the pulse and the presence of other signs of such failure. Again, an urgent form, met with in renal cases, may result from pulmonary œdema, and is attended by profuse, frothy expectoration which is apt to be blood-stained. This, again, although a renal rather than a uremic event, is not uncommonly met with in association with more strictly uremic phenomena. Pneumonia, hydrothorax, and hydropericardium must also be mentioned as causes of dyspnœa in renal cases, and the rarer œdema of the larynx which occasions urgent respiratory distress.

To a different category from those so far mentioned belongs the condition known as "uremic asthma," which occurs in a paroxysmal manner; in this as in ordinary asthma, the dyspnœa is mainly expiratory. No

physical signs are to be detected apart from stridor. Such an attack is apt to supervene in the later stages of chronic renal disease, and in cases of granular kidney may be of sudden onset; it is not necessarily preceded by any serious indications of impairment of health. A great increase of pulse tension is characteristic of uremic asthma, and serves to distinguish the condition from other varieties of dyspnoea in the uremic state. This point is very clearly brought out by M. Weiss<sup>1</sup> in his admirable description. In some instances the vasomotor storm is preceded by a stage of vascular relaxation with a resulting peripheral hyperemia, but upon this the stage of spasm quickly supervenes.

Among the respiratory symptoms periodic breathing of the Cheyne-Stokes variety claims a place. The occurrence of Cheyne-Stokes breathing in uremia is by some attributed to cardiac failure, which is certainly one of the more common causes of such dyspnoea. However, there are difficulties in the way of accepting this explanation without qualification, and it is at least possible that when in an early symptom of uremia the sluggish response of the respiratory centre may have a toxic origin.

**Temperature.**—In chronic uremia the body temperature tends to be subnormal. In some instances the fall is very conspicuous and subnormal readings are often continuously observed. On the other hand, febrile disturbance is usually present in association with acute attacks, and this, apart from any obvious complications such as pneumonia or pericarditis. The fever may even attain to hyperpyrexia. Strümpell, who attaches considerable prognostic importance to the state of the body temperature, regards exceptionally high or exceptionally low readings as of very unfavorable significance, whereas the outlook is decidedly better when the temperature does not depart very widely from the normal in either direction. This opinion is borne out by experience.

**Cutaneous Lesions.**—*Itching*, which may be intense, is a not uncommon symptom, and, owing to the presence of urea in the sweat, the skin may be covered with a crystalline efflorescence of that material. With these exceptions, skin affections must be classed among the rarer manifestations. However, there are strong reasons for including a form of erythematous eruption among the symptoms, for it has repeatedly been observed as a precursor of the more usual manifestations, or in association with these, in cases which have shortly afterward ended fatally. Le Cronier Lancaster<sup>2</sup> described this rash as first appearing in discrete maculae of a bright red color, usually upon the extensor surfaces of the hands, forearms, and legs. These quickly become papular, and fresh maculae and papules appear on all parts, including the face, palms, and soles. The mucous membranes are also affected and the throat becomes sore and congested. The papules tend to become confluent over large areas, especially on the back, arms, and thighs. After the lapse of three or four days the eruption may subside and extensive and free desquamation may follow, leaving the skin of a dull red tint and brawny, while some of the papules may become hemorrhagic. Sometimes the rash assumes an eczematous character, with the formation

<sup>1</sup> *Zeitsche. f. Heilkunde*, 1881, ii, 79.

<sup>2</sup> *Clinical Society's Transactions*, London, 1892, xxv, 49.



of scabs and crusts, and pustulation may occur. As a rule, itching is a prominent symptom. The prognostic significance of the erythema is decidedly evil and death usually follows within a few weeks.

**The Symptoms which Result from Anuria.**—Whereas lesions of both kidneys which bring about conspicuous impairment of their functions usually result, sooner or later, in the development of uremia, it is a very remarkable fact that, when the excretory functions of both kidneys are completely suspended, the symptoms observed are not those of ordinary uremia, and are comparatively slight, although, if the anuria persist, a fatal ending is, after no long interval, inevitable. The cases in which such a condition is most often observed are those in which, one kidney having been previously rendered useless owing to obstruction of its ureter, a calculus lodges in the ureter of the remaining kidney. Less frequently both ureters are simultaneously obstructed by calculi or involved in a new growth. However, a similar result is brought about by thrombosis of both renal arteries.

In a large proportion of cases of obstructive suppression some urine is passed at times, presumably because the pressure behind the obstacle reaches a level at which some of it is able to pass. Such urine is very pale, of low specific gravity, and contains little urea or other excretory products. It is sometimes blood-stained. The occasional passage of urine having the above characters affords little relief and does not long postpone the end. Obstructive suppression, unless it be relieved by the passage of a calculus or by surgical procedures, is necessarily fatal, but as many as seven or eight days may elapse before conspicuous symptoms develop. Although life may be prolonged for three weeks, death commonly supervenes in from nine to eleven days from the onset.

During the earlier days the patient may exhibit hardly any symptoms suggestive of grave illness. Sleeplessness and gastric disturbance are usually present, but there may be no headache or vomiting. Progressive muscular weakness is common; the mind usually remains clear. Of the symptoms of the later days, dryness of the mouth and tongue, contraction of the pupils, and muscular twitching are among the most prominent and most constant. Convulsions are absent. The patient may become more and more drowsy and there may be some delirium, but coma is rare, and in not a few cases the patient remains fully conscious up to the moment of death. The appetite may be maintained up to within a few days of the end, but at the last usually fails completely. Curiously enough, the ammoniacal urinous odor which is so commonly noticed in uremia is wanting in cases of obstructive suppression. The breathing is slow and difficult. The pulse rate is little affected or is slightly quickened toward the end; the temperature tends to fall below the normal level during the later days.

**The Classification of Uremic Attacks.**—Attacks of uremia may be classified according to their most prominent symptoms as nervous, alimentary, or respiratory, and so much is some special class of symptoms wont to predominate in individual cases that a classification upon such lines seldom presents any difficulty. More commonly the cases are grouped as acute, chronic, or latent, and the subdivision of the acute

cases into acute and fulminating; suggested by Rose Bradford, has a sound clinical basis.

*Fulminating* uremia most commonly occurs in the course of chronic renal diseases. A patient with granular kidneys, who may not be conscious of any serious impairment of health, is suddenly attacked with uremic convulsions, which may even prove fatal in the course of a few minutes, or by urgent uremic dyspnoea; again, a sufferer from that form of nephritis which is associated with contracted white kidneys develops acute uremic symptoms with little previous warning. In the acute form which may develop in cases of acute nephritis, and is also occasionally seen after operations upon the lower urinary tract, such as dilatation of a stricture, convulsions may occur after a short premonitory period in which headache, vomiting, dyspnoea, or delirium are the most prominent manifestations.

*Chronic* uremia is best seen in cases of chronic parenchymatous nephritis, in which the minor symptoms of the condition, such as nausea, vomiting, and sometimes diarrhoea, may precede by a considerable period the onset of graver manifestations, and may persist for weeks.

The name *latent* uremia is applied to the condition met with in cases of obstructive anuria, in which the more characteristic uremic symptoms may be absent up to the fatal ending.

**Diagnosis.**—The diagnosis of uremia presents difficulties in not a few cases. Thus, when a patient is seen for the first time in a condition of coma, other varieties of coma have to be excluded. This is done by consideration of the state of the patient and by the history of his illness. The state of the pupils, as to equality, dilatation, or contraction, the odor of the breath, the presence or absence of albumin in the urine, the tension of the pulse and state of the arteries, and the presence or absence of evidences of paralysis of limbs, all need to be taken into account in arriving at a diagnosis. The history of a convulsion at the onset is very important, but it must not be forgotten that a series of convulsions followed by prolonged unconsciousness may occur in epilepsy and in the course of general paralysis of the insane, and that albuminuria may follow convulsive attacks. Difficulties of another kind may arise from the protean nature of the attacks, and the prominence of some particular symptom which may be one of the less common ones. Thus in one case vomiting may be almost the only symptom, in another hiccough. An attack may be ushered in by delirium which may even be maniacal, and Cheyne-Stokes breathing may be the earliest symptom. Hence, when any symptom of the uremic group is met with in patients suffering from renal disease its uremic origin is to be suspected.

**Prognosis.**—This is always grave, and in connection with it two main points have to be considered—namely, the chance of recovery from the actual attack, and the likelihood of a recurrence of uremia at an early date.

In acute nephritis with almost complete suppression of urine the patient may die during an attack of acute anuria, but, on the other hand, a patient who has exhibited grave uremic symptoms, such as convulsions followed by coma and amaurosis, may nevertheless make a

complete recovery, the danger of recurrence being wholly averted. On the other hand, in cases of chronic nephritis, even though the danger be averted for a time, a recurrence is highly probable, or, indeed, almost inevitable, at no very distant date, and in the great majority of cases the attack, if not at once fatal, marks the commencement of a rapid downward progress. The immediate prognosis of the attack depends in part upon the violence of the symptoms, for the fulminating attacks are usually fatal, and in part upon the response to our efforts to improve the working of the kidneys and to eliminate the poison by other paths. In latent uremia a fatal ending is inevitable unless it is possible to restore the functional activity of the kidneys.

**Treatment.**—The methods which have met with general acceptance are, for the most part, based upon the assumption that the poison at work is a nitrogenous product which fails to be adequately excreted by the diseased kidneys. Thus the attempt is made, by restrictions of diet, to limit the formation of the end products of protein katabolism, and at the same time to reduce the accumulation of such products in the blood by venesection, and by encouraging their vicarious elimination by other channels than the kidneys.

Many patients who develop uremia are already under treatment on account of the primary renal disease, and appropriate treatment of the nephritis offers the best chance of averting the onset of uremia. In cases of acute nephritis in which the output of urine is scanty, as also in cases of parenchymatous nephritis in which headache and vomiting or other symptoms of incipient uremia are beginning to manifest themselves, the application of dry cups to the loins will often prove of much service and is usually followed by a conspicuously increased output of urine.

Copious *diaphoresis* is an important and well-established method of treatment. It has been objected that the quantity of excretory products, as measured by urea, which can be thus vicariously removed, is comparatively small, and that profuse sweating will tend to increase their concentration in the blood. However, clinical experience teaches us that hot water baths, and hot air or vapor baths, have a decidedly beneficial effect in uremic cases, and the pathology of the conditions is still so obscure that it would be very unwise to abandon a plan of treatment of proved utility for merely theoretical reasons.

In acute cases, in which a prompt and copious diaphoresis is aimed at, the subcutaneous injection of nitrate of pilocarpine in doses of  $\frac{1}{6}$  grain (gm. 0.01) may be resorted to, but is now regarded with less favor than formerly. In connection with diaphoresis, as with other plans of treatment, the condition of the individual patient needs to be carefully considered, and especially the state of the heart and character of the pulse. The pulse should be carefully watched during the administration of the sweat bath, and stimulants should be given if necessary.

Hydragogue cathartics are of undoubted service. In the more chronic cases saline purgatives or compound jalap powder, aided, if necessary, by enemata, will usually suffice, but in acute attacks more drastic cathartics, of which elaterium is most in favor, are called for. The utility of purgation is probably only in small part due to the



comparatively scanty elimination of waste products by the bowel. Vomiting, which is so common a symptom, aids the vicarious elimination, and lavage of the stomach has been recommended with the same object in view. *Venesection*, with the withdrawal of 12 to 20 ounces of blood, proves of great service in not a few cases, and is regarded by some physicians as by far the most important of all the therapeutic measures employed in uremia. Whether or not bleeding should be resorted to will be largely determined by the state of the pulse, and when a pulse of conspicuously high tension is a prominent feature, venesection will commend itself, rather than in cases in which a soft and feeble pulse affords evidence of a failing heart. The benefit which results is thought to be largely attributable to the withdrawal of a portion of the toxic material in the shed blood. Infusion of normal saline solution to replace the blood withdrawn is frequently practised, and in cases in which oedema is absent, as in acute uremia in connection with granular kidneys, saline infusions, apart from venesection, have been recommended.

Removal of cerebrospinal fluid by lumbar puncture has recently been employed with benefit.

For the reduction of excessive pulse tension, nitroglycerin, or in acute attacks the inhalation of nitrite of amyl, may be employed; but even in uremic dyspnœa, in which high tension plays so conspicuous a part, these drugs may afford but little relief. Digitalis is often of service in chronic cases, both in virtue of its action as a cardiac tonic and as a diuretic. Inhalation of oxygen, and especially its continuous inhalation, is of very real service in the treatment of uremic dyspnœa, and is strongly recommended by Samuel West as calming the distressing restlessness and even as modifying convulsive attacks.

For the control of convulsions inhalation of chloroform is usually very effectual, and chloral and bromides may be administered either by the mouth or the rectum. Morphine, the use of which has been strongly recommended by Stephen Mackenzie, Osler, and others, often proves most valuable in the treatment of uremic states, and its judicious use has been shown to be unattended by the dangers which were formerly regarded as contra-indicating its employment. In renal dyspnœa it is said to afford more relief than any other therapeutic agent, and it also gives relief from restlessness, insomnia, and such conditions as the mental disturbances and Cheyne-Stokes dyspnœa which usher in the onset of uremia in some cases of granular kidney.

## CHAPTER XV

### NEPHRITIS: INTRODUCTION AND ETIOLOGY—ACUTE NEPHRITIS

By JAMES B. HERRICK, M.D.

**Introduction.**—By nephritis is meant an inflammation of the kidney, and, as the term is commonly employed, a non-suppurative inflammation is implied. If other than the non-suppurative form is meant, a qualifying adjective, as “suppurative,” “pyelo,” etc., is prefixed. Non-suppurative nephritis is often spoken of as Bright’s disease, or morbus Brightii, the terms nephritis and Bright’s disease being used interchangeably. Strictly speaking, this is not correct. Bright described those inflammations of the kidney accompanied by albuminuria and dropsy, so that his description did not include the group of nephritides in which there is no dropsy. So, too, in reality, it is not correct to speak of some of the diseased conditions commonly referred to as nephritis as inflammations of the kidney, *i. e.*, as exudative and proliferative in character. The granular atrophy, for example, is, in the strict sense, not an inflammation. But until clinical and pathological differentiation is more sharply defined, the term nephritis, or Bright’s disease, may conveniently be employed to designate the non-suppurative inflammations of the kidney, it being tacitly understood that some forms of “nephritis” are degenerative or atrophic in character rather than inflammatory, and that some conditions called Bright’s disease are different from anything actually described by Bright.

There is a quite general agreement as to the division of all cases of nephritis into the two classes of acute and chronic. Clinically and anatomically the distinction between acute and chronic is not always clear. Subdivisions of the *acute* class into varieties are occasionally attempted, sometimes on an etiological basis, *e. g.*, malarial nephritis, or sometimes on a histological basis, *e. g.*, glomerular or tubular nephritis, but such subdivisions will not be very satisfactory until etiological classification becomes possible.

No serious, at least no successful, attempt has ever been made to classify cases of *chronic nephritis* from the stand-point of etiology. Morbid anatomists and pathologists are far from unanimous in their descriptions of the various types or groups of this disease. And physicians are not always able to make a differentiation that is satisfactory from the clinical point of view or that holds good in the light of postmortem revelations. Yet it is important that we have some working classification, even though it be somewhat faulty and largely artificial.

From the time of Bright (1827) down to the present there has been

more or less confusion of ideas concerning chronic nephritis. Rayer, a few years after Bright's first paper, made four varieties of chronic nephritis. In 1867 Rindfleisch declared that "the pathological anatomy of the kidney is certainly the subject which has stimulated the most investigation, and yet today it is the least complete chapter of the whole work." And Bartels,<sup>1</sup> a little later, besides quoting with approbation the sentence from Rindfleisch, adds that "it is apparent that the doctrine of the diffuse renal diseases cannot be regarded as settled from any point of view." Senator,<sup>2</sup> writing in 1901, says: "There is at present no detailed classification that has met with general approval and acceptance." Bradford<sup>3</sup> (1901) says: "Chronic Bright's disease, however, is the form in which the greatest diversity of opinion, as to its nature and forms, exists."

At the meeting of the German Pathological Society in 1905 there was a general discussion on morbus Brightii. Ponfick,<sup>4</sup> in a leading paper, emphasized the importance of further careful correlated clinical and anatomical study of cases, so that more order might be brought out of the present confusion. Friedrich Müller,<sup>5</sup> in an inspiring and masterly critique of recent views concerning Bright's disease, admitted the unsatisfactory nature of our knowledge concerning the true character of the lesions in the kidney, our loose methods of classification, the difficulties to be overcome before an exact etiological classification is possible, and our use of a terminology that is neither historically, clinically, nor anatomically correct. He even proposed the use of a new term, "nephrosis," to include in a comprehensive way the degenerative lesions of the kidney that could not, strictly speaking, be called "nephritis."

It may be stated that the *kidney of congestion* is, by common consent, ruled out of the category of the nephritides and Bright's disease. *Amyloid kidney* is now rarely classed as a form of Bright's disease, or as an inflammation of the kidney, although it is recognized as occurring not infrequently in connection with, or as a complication of, a true nephritis. There remain two groups of the chronic nephritides whose clinical features present such striking contrasts that, for purposes of description, one feels warranted in making separate classes of these groups. The justification of this seems apparent when one sees that corresponding to these two types, kidneys are found differing as markedly as do the clinical manifestations. To the one form, characterized by cedema with abundant albuminuria and cylindruria, the name *chronic parenchymatous nephritis* has been most often applied; to the other, with its marked cardiovascular changes, its relatively slight albuminuria and cylindruria, with its abundant urine of low specific gravity, its frequent uremia, the term *chronic interstitial nephritis* is given. As synonyms for the former may be mentioned large white kidney, large yellow kidney, chronic desquamative and chronic tubal nephritis, etc.; for the latter, contracted

<sup>1</sup> Ziemssen's *Encyclopædia*, American edition, xv, 187.

<sup>2</sup> *Die Erkrankungen der Nieren*, Zweite Auflage, Berlin, 1902, p. 194.

<sup>3</sup> Diseases of the Kidneys in *Gibson's Practice of Medicine*, 1901, ii, 316.

<sup>4</sup> *Verhandl. der deutsch. path. Gesells. Centrabl. f. allg. Path. und path. Anat.*, 1906, Band xvi, 49-64.

<sup>5</sup> *Ibid.*, pp. 64-99.



kidney, cirrhosis, sclerosis, granular atrophy, gouty kidney, etc. The former is the "large white kidney." The kidney of the second class is the "contracted kidney."

While these are types and while they are seen with all their classical text-book features, both at the bedside and on the autopsy table, great variations are frequently met with. Heubner rightly says that the majority of chronic kidney conditions are, according to generally accepted types, atypical. On close examination, it is seen that the names parenchymatous and interstitial are in reality misnomers, for with every parenchymatous nephritis the interstitial tissue is involved, and parenchymatous changes are seen in every case of chronic interstitial nephritis. The process is in reality a diffuse one—a *chronic diffuse nephritis*. In the one case the parenchyma is chiefly, and perhaps primarily, involved, and there is little or no induration or contraction; in the other, the interstitial structure shows the chief, perhaps the primary, change, and there is contraction or induration. Hence we have Senator's two classes of (1) chronic diffuse nephritis without induration; (2) chronic diffuse nephritis with induration. By diffuse is not meant that every part of the two kidneys—Bright's disease being a bilateral affection—is involved; as is well known, circumscribed foci of inflammation are often a striking figure in the kidney of nephritis, the "patchy" areas showing pathological change contrasting strongly with the healthier areas. By diffuse is meant diffuse in the sense that the parenchyma and interstitium are both involved.

In practice the cases do not permit of such easy distribution into appropriate pigeon-holes as one might think. The pathologist often refuses to say more than that there is a chronic nephritis; and the clinical manifestations may be a mixture of the findings of the two classes. We must often be content with the diagnosis of chronic nephritis or chronic diffuse nephritis. This point deserves special emphasis, for much energy is wasted and much needless disappointment experienced in the attempt to make a given case fit into a classification that is largely artificial and necessarily imperfect. It is better for teacher, student, and practitioner to have a frank understanding and to realize that disease often refuses to conform to the picture of the classical type.

In some cases the view of Frerichs and of Reinhardt that the contracted kidney is a later form of the parenchymatous seems to be confirmed. At the bedside this transformation of a chronic parenchymatous nephritis into the chronic interstitial is occasionally seen, and at postmortem a condition of secondary contraction is recognized. If we preserve the term chronic interstitial nephritis for the indurated or contracted kidney, it might be well to adopt the expressions *secondary interstitial nephritis* for this form and primary interstitial nephritis for the slowly developing, insidious, cardiovascular, typical contracted kidney. As a subhead under chronic interstitial nephritis should be placed the *arteriosclerotic kidney* or granular kidney, with its striking local vascular changes that are but a part of a more general arteriosclerosis. This can generally be recognized at autopsy, and may be suspected and permits of a probable diagnosis during life, particularly in the aged.

The classification that seems the best is practically that of Senator:

1. Chronic parenchymatous nephritis. (Chronic diffuse nephritis without induration.)
2. Chronic interstitial nephritis. (Chronic diffuse nephritis with induration.)
  - (a) Primary chronic interstitial nephritis.
  - (b) Secondary chronic interstitial nephritis.
  - (c) Arteriosclerotic kidney.
3. Mixed type, a combination of 1 and 2, *i. e.*, diffuse nephritis.

### ETIOLOGY OF NEPHRITIS

In some instances the kidney is involved by a *direct extension* of inflammation from a neighboring structure. Such, for example, is the case in the ascending nephritis consecutive to pyelitis—pyelonephritis.

But in the great majority of cases some substance carried by the blood to the kidney acts as the excitant of inflammatory or degenerative changes, acute or chronic, as the case may be, and the result is a nephritis or an atrophic process that in its results is akin to a true nephritis. These causes may for purposes of description be classified, although the distinctions are here somewhat artificially made; and in reality the operating etiological factor in a given case is often not a simple one but a combination of two or more of the causes mentioned in these different groups. A working classification may be made as follows:

1. The infectious diseases, acute and chronic.
2. Chemical, *i. e.*, toxic substances, acute or chronic in their action.
  - (a) Exogenous.
  - (b) Endogenous. (i) Gastro-intestinal. (ii) Metabolic products.
3. Cold. *Nephritis à frigore*.
4. Pregnancy.
5. Heredity.

1. **The Infectious Diseases.**—Infectious diseases may as a class be regarded as the cause of a large percentage of cases of acute nephritis. Many cases that at first sight seem to be due to causes that are not microbic, often on close analysis are found to have been preceded by definite symptoms of an infection, mild perhaps or even unheeded by the patient, but yet presumably the *fons et origo* of the later renal complication. An ambulatory scarlet fever, a comparatively insignificant angina, a mild rheumatism, a "cold" or supposedly trifling "la grippe" may be the precursor of a nephritis. In cases of obscure origin the cause may lie in an unsuspected pus focus in a tonsil, at the root of a tooth, in the gall-bladder, middle ear, urinary bladder, etc. The slow absorption of small amounts of toxins from these foci may have rendered the patient in a sense immune so that there are no very striking symptoms, either from the original source of the infection or in the kidney or other tissue that is secondarily involved; the process may rather be subacute. Such a patient may be said to have, as Dr. Kirk has well put it, the "toxin habit." He has become accustomed to and tolerates fairly well the ordinary dose of toxin absorbed.

Among the infectious diseases attended or followed by acute nephritis *scarlet fever* stands preëminent. Even before the time of Bright, clinicians had noted the now well-recognized complication. Without stating it in figures, it is sufficient to know that experience the world over, in hospitals and in private practice, and with various kinds of treatment, has demonstrated the great frequency with which scarlet fever is accompanied by acute inflammation of the kidneys. There would seem to be some selective action on the part of the infectious or toxic agent present in this disease for the kidney and even for one particular part of the kidney, viz., the glomerulus. Often the other clinical manifestations of scarlet fever are on the wane or have entirely disappeared; often the whole course of the illness has been mild, yet the nephritis occurs. Why the kidneys should be so peculiarly vulnerable in this malady is not known. Undoubtedly in some cases of scarlatinal nephritis there is a combination of operative causes. While the toxin must be regarded as the primary cause, exposure to cold, errors in diet, too short a period of rest in bed, constipation, or the use of alcohol may assist.

Disregarding febrile albuminuria, acute nephritis is by no means as common in *diphtheria* as in scarlet fever. Acute nephritis in this disease is manifested in much the same manner as in scarlet fever, although it is more apt to make its appearance earlier. Since the use of antitoxin it is of rarer occurrence, it may be interesting to note that one of the earlier proofs that it was the toxin in many infectious diseases and not the organisms themselves that induced the nephritis was afforded by the injection of diphtheria toxin into animals, with the subsequent development of nephritis.

Bright's disease as a complication of the other common infections of childhood is comparatively rare. Yet occasionally it is seen in *measles*, *German measles*, *chicken-pox*, *whooping cough*, and *mumps*. It may occur in *epidemic cerebrospinal meningitis*.

A trace of albumin with a few casts is a common finding in *typhoid fever*, disappearing with the subsidence of the fever. True nephritis is rare, and Bartels<sup>1</sup> saw but two instances in 1000 cases. The renal symptoms may appear early and for a time be the most striking feature of the case, constituting the so-called renal typhoid, or, it may be later, during the height of the disease or as convalescence sets in, that the kidney may become involved. In *pneumonia* casts and albumin can usually be found. In a series of consecutive cases the writer found in each instance at some time during the illness a trace or more of albumin and a few hyaline or granular casts. True nephritis is comparatively rare. It may appear during the height of the disease or during convalescence. In some of the cases of acute nephritis found in pneumonia, as in other infections, the renal trouble is merely an aggravation of a previously existing chronic nephritis, *i. e.*, an acute exacerbation.

With *typhus fever* and *smallpox* acute inflammation of the kidney is common. It has been seen in *vaccinia*. In *cholera* the scanty, bloody, and albuminous urine is found associated with an acute destructive

<sup>1</sup> Ziemssen's *Encyclopedia*, xv, 527.



degenerative change in the kidney. In *yellow fever* and *acute yellow atrophy of the liver* acute degenerative and inflammatory lesions are frequently found in the kidneys, and the symptoms of acute nephritis are present. In *relapsing fever* acute nephritis has been noted (Ponfick).

*Malaria* often induces nephritis apart from the hemoglobinuria or black-water fever. Kelsch and Kiener insist upon the occurrence of malarial nephritis. Thayer analyzed the Baltimore cases and found acute nephritis in over 4 per cent. of the patients with estivo-autumnal infection. The so-called febrile albuminuria is found in a much larger percentage—probably one-half—of the cases of acute malaria.

Considering the great frequency of *rheumatic fever* and *chorea*, nephritis must be regarded as a rare complication of these diseases, yet it is occasionally seen. If, however, we regard some of the anginas of obscure origin and some of the *purpuras* as rheumatic in character, rheumatism must be looked upon as a not infrequent cause of nephritis. It is not unusual to see a patient whose illness began with sore throat, joint pains, and purpuric manifestations, in whom œdema, albuminuria, hematuria, cylindruria, etc., give unmistakable evidence of an acute nephritis. In *erythema nodosum*, also, nephritis is reported.

As has been already said, a *tonsillitis*<sup>1</sup> or an every-day sore throat is in many instances the atrium for the entrance of toxic infectious agents that induce nephritis, and in all cases of obscure origin careful inquiry should be instituted as to recent throat or nose trouble.

With *erysipelas* febrile albuminuria is common; true nephritis occurs, although not often. Nephritis has also been reported in *dysentery*.

With *septicemia* and *pyemia*—due to a streptococcus, staphylococcus, pneumococcus, gonococcus, etc.—febrile albuminuria is the rule. True nephritis also is not uncommon. In some instances the nephritis is clearly metastatic, mycotic emboli from a thrombosed vein or from infected cardiac valves lighting up the nephritis or perhaps producing a suppurative nephritis or surgical kidney. But aside from the embolic variety, acute nephritis—"toxic infectious"—in the course of sepsis is frequently seen. Possibly some of the instances in which nephritis is recorded as due to a *skin disease* are in reality of the nature of "toxic-infectious" inflammations, the skin lesion being suppurative or furnishing a portal of entrance for germs. In a similar way *alimentary disturbances* may be microbic and the nephritis that perchance results might be classed under the head of infectious, although toxins are probably the direct exciting cause.

Acute or subacute parenchymatous nephritis is often seen in *tuberculosis*. Some of the supposed cases of nephritis with tuberculosis are amyloid. Perhaps, too, secondary infection with pyogenic microbes explains some of the cases of Bright's disease complicating tuberculosis. But whether one looks upon the tuberculous toxin as the cause of the complication, a view that has some experimental and clinical support, particularly from French observers, or regards the tuberculosis as merely a predisposing cause, and exposure to cold, use of drugs, overfeeding,

<sup>1</sup> Cf. Morse, *Archives of Pediatrics*, 1904, xxi, 337.

use of alcohol, or a secondary infection as the real cause, certain it is that nephritis is quite common in tuberculosis.

*Influenza* is also a cause of nephritis. During the epidemic in the nineties the unusually large number of cases of acute nephritis excited general comment among practitioners.

Occasionally cases have been seen in which the question of the existence of some *specific germ* for acute nephritis has been raised. Saundby cites Fiesinger,<sup>1</sup> who described what appeared like an epidemic of nephritis, no other localization of the infection than in the kidney being manifest. Black Milne<sup>2</sup> raises the question as to the possible specific microbic origin in certain cases with a special tendency to localization in the kidney.

The controversy concerning *syphilis* as a cause of nephritis has not yet quieted down. There are those who regard the inflammation of the kidneys in a syphilitic as due to the drugs employed, especially the mercury, to the influence of cold (Bradford), to accidental causes, such as alcoholism, to other infections, etc. Klieneberger,<sup>3</sup> in Lichtheim's clinic, made a careful urinary study of 31 patients, some of whom were non-syphilitic, who were treated by mercurial inunctions. With great uniformity he found evidence of irritation of the kidney in the presence of albumin and casts, and while advocating the use of mercury in the treatment of syphilis, he feels that the remedy should be used cautiously and the effects on the kidney carefully noted, for, as he says, this is not an "indifferent" treatment. Wagner suggested that the angina often seen in syphilis might be the intermediate agent in producing nephritis by affording an avenue of admission for harmful germs. It is difficult to settle the question on the basis of clinical evidence alone. The writer's experience tallies with that of those who regard syphilis as a potent cause of acute nephritis, especially in the first two years after the initial lesion.<sup>4</sup> Of the influence of syphilis in producing chronic sclerotic changes in general, including such changes in the kidney, there is little question.

The fact that an acute inflammation of the kidney accompanies or follows hard upon an infectious disease does not of necessity prove that the particular microörganism producing the infectious disease or its toxins is also causing the nephritis. While this is presumably so, it may often be that the infectious disease merely paves the way for some secondary and intercurrent microbic or toxic agent that acts upon the kidney under these, for the kidney, unfavorable conditions. Nothing definite is known that will explain why in one case of acute infectious disease the kidneys escape, while in another they are hard hit. Variations in the amount of the toxin, its virulence, or the length of time it acts must be assumed to aid in the explanation. Differences in the make-up of the kidney and its resisting power or sensitiveness to harmful influences, and differences in the resisting power of the body as a whole, must be inferred. A once damaged kidney may be peculiarly liable to

<sup>1</sup> *Rev. de Méd.*, 1893, p. 404.

<sup>2</sup> *Brit. Med. Jour.*, 1892, ii, 1391.

<sup>3</sup> *Zeitschr. f. klin. Med.*, 1906, lviii.

<sup>4</sup> The subject of syphilitic nephritis has been treated by Jossierand, *Lyon Médical*, November, 1904. Cf. Max Wagner, *Munch. Med. Woch.*, 1902, Nos. 51 and 52, which contain numerous references.

become again seriously affected. Recovery may have ensued in a clinical or functional sense, yet a recovery with some permanent weakness or defect. But the entrance again into the body of microbes or the springing into activity of microorganisms that have long lain dormant and apparently harmless in the body—typhoid bacilli in the gall-bladder, gonococci in the prostate or Fallopian tubes, streptococci or staphylococci in the middle ear or in an ancient osteomyelitis or tonsillitis—may lead to a fresh acute outbreak in the kidney that had apparently recovered, but now shows itself peculiarly sensitive to even slight insults.

A selective affinity of the toxins of certain diseases, *e. g.*, scarlet fever, for the kidney may also be assumed to explain the unusual frequency of Bright's disease with some infections, its rarity with others. And the organisms, or rather their toxins, often display a selective affinity for certain parts of the kidney, one organism damaging particularly the glomeruli, another the tubular epithelium, or another the interstitial tissue. The lesions, too, are with some organisms chiefly exudative and proliferative *i. e.*, truly inflammatory, with others degenerative or again often characterized by hemorrhages or interstitial cellular accumulations. More experimental, histological and clinical observation is still needed in order to clarify our knowledge of the anatomical changes, the perversion of function and the clinical manifestations due to acute nephritis as produced by particular kinds of organisms.

**2. Toxic Agents.**—While the true nature of the poisons that produce nephritis in the case of the infectious diseases is not known, and while many of the more strictly toxic nephritides are due to poisons whose origin in the body is obscure and whose chemical composition is still unrecognized, there are certain known toxic substances that are capable, when introduced into the body in large enough amounts, of producing an acute nephritis; and others capable of inducing a chronic change in the kidney, provided the action be extended over a long period of time.

(a) **Exogenous Toxic Substances.**—Of the exogenous toxic substances a long list might be given, including certain organic and inorganic chemicals used as *drugs*, and others whose entrance into the body is always a matter of accident or due to an intent to harm. Such substances are cantharides, turpentine, carbolic acid, chlorate of potassium, salicylic acid and its compounds, oxalic acid, the mineral acids, bichromate of potassium, alcohol, chloroform, phosphorus, mercury, lead. Long-continued action of many of these substances in smaller amounts, *e. g.*, lead or mercury, may induce chronic nephritis. Morphinism may be a cause. Even chloride of sodium, which has at times been employed for the production of inflammatory and degenerative lesions of experimental nephritis (Stokvis, Levi, Castaigne and Rathery), has been regarded as an occasional cause of acute nephritis<sup>1</sup> when used in large doses. The innocuousness as regards the kidneys of the curative *sera*, of tuberculin, of vaccine virus, etc., is one of the fortunate facts concerning these valuable diagnostic and therapeutic agents, but whether in exceptional instances a toxic nephritis may not be lighted up is not definitely settled.

<sup>1</sup> Cf. Tarino, *La Presse Médicale*, 1904, xxviii, 222.



The effect on the kidney of the injection of the vaccines in the treatment along the lines of the so-called "opsonic therapy" of Wright must also be carefully watched. In *ptomaine* poisoning damage may be done to the kidneys by ingested poisons. The whole question of the effects of adulterated food on the kidneys is one requiring careful consideration, and the use of such adulterants calls for proper legal restrictions. The question may also be raised whether at times a nephritis may not be induced by the excessive quantity of food, *e. g.*, meat, that is eaten, overwhelming the kidneys by the quantity rather than the quality of the digestive and metabolic products. The too free use of highly seasoned foods has also been held responsible for some cases of nephritis.

The exogenous toxic substances do not always enter by way of the alimentary tract. Chloroform and ether may be a possible excitant of nephritis, even when inhaled. The external application of drugs has in numerous instances been held responsible for inflammation of the kidney. Care should always be exercised in the use on the skin, and particularly when the surface of the skin is broken, of such remedies as carbolic acid, turpentine, bichloride of mercury, iodoform, pyrogallic acid, naphthol, and the preparations of tar. Acute nephritis has been reported in which the cause seemed to be the extensive application of balsam of Peru.<sup>1</sup> Gassmann<sup>2</sup> gives references to some six or seven cases in which balsam of Peru externally applied produced acute nephritis.

In some lesions of the skin, such as eczema, the nephritis that is occasionally seen as an accompaniment is perhaps due to the formation of some toxic product in the diseased skin. Extensive burns,<sup>3</sup> as is well known, are peculiarly prone to be followed by acute, often severe, changes in the kidney due to toxic substances resulting from the destruction wrought in the skin. Some, however, regard the hemolytic changes in the blood through the agency of the burn as the cause of the toxic symptoms and of the anatomical alterations. The intestine and kidneys are the chief avenues of elimination of this poison, and often show the most marked pathological lesions. The poison is in some respects comparable to the snake venoms.

The long-continued use of the *Röntgen rays* may not be without harm to the kidney. This probably arises more from the destruction of leukocytes and of lymphoid or neoplastic tissue, with the development of toxic substances that are injurious to the kidney, than from the direct harmful effect of the ray upon the kidney itself. Warthin<sup>4</sup> describes inflammatory and fibrotic changes with remarkable lime-salt deposits in the kidneys of patients with myeloid leukemia and Hodgkin's disease who had been treated for a long time with the Röntgen rays. The necessity of careful watching of the urine in such patients is clear.

(b) **Endogenous Toxins.**—Most of the endogenous toxins are as yet unidentified, but it is possible that not a few of the cases of acute nephritis may be due to toxic substances rapidly formed within the body.

<sup>1</sup> L. H. Hoffman, *Jour. Amer. Med. Assoc.*, 1907, p. 2086.

<sup>2</sup> *Münch. med. Woch.*, 1904, No. 30.

<sup>3</sup> Literature on burns in Pfeiffer, *Virchows Archiv*, 1905, clxxx, 367.

<sup>4</sup> *Am. Jour. Med. Sc.*, 1907, cxxxiii.

(i) Acute gastro-intestinal disorders at times seem to be the starting-point of acute nephritis. Here, in many instances at least, micro-organisms or irritant chemicals have been introduced from without, but the disturbed conditions in the alimentary tract give rise to the formation of new toxic products which when absorbed act harmfully upon the kidney. Acute nephritis of this type, *e. g.*, occurring in connection with the acute gastro-enteritis of children, is a good illustration of the frequent combination of causes of various kinds, microbic and chemical, exogenous and endogenous. It does not seem a rash assumption regarding many cases of chronic nephritis of otherwise obscure origin to look upon *digestive disturbances* as the etiological factor. Errors in diet and digestive functions faultily performed may easily be regarded, if continuing for a long period, as leading to chronic toxemias, with resulting renal changes. In some instances bacterial growth in the bowel may be excessive and toxins increased in quantity, or the change may be qualitative rather than quantitative, the bacteria being different in kind. Or we may conceive of some protective chemical process in the bowel or liver as being deficient under pathological conditions, and a toxin that in health is rendered harmless, being absorbed, reaching the kidney and inducing inflammation. Suggestive experimental work along this line of the combined action of chemical and microbic causes has been done. O'Hare,<sup>1</sup> by combining the action of uranium nitrate and the colon bacillus, was able to produce in rabbits a lesion similar to that of chronic nephritis in man.

In children malnutrition with its gastro-intestinal disturbances may cause nephritis. This is seen in infants in hospitals and asylums.<sup>2</sup>

(ii) When we broaden the conception so as to take in *disorders of metabolism* we may find a probable explanation for many chronic nephritides. But little definite knowledge is as yet possessed upon this subject. Still, one may imagine that faults on the part of such organs as the liver, pancreas, adrenals, thyroid gland, or even the muscles, might by mal-performance of function, perhaps internal secretory function, lead to chronic renal disease. And the influence of excessive worry, anxiety, business hurry, and *nervous* strain in the production of chronic nephritis, a fact regarded by many as explaining the apparent frequency with which Bright's disease is seen in modern life, may be due to faulty performance of function on the part of some of the viscera through perversion of nervous influence, or even to the presence in undue amount of some obscure toxic material, the result of excessive overuse of nerve cells.

With *jaundice*, albumin and casts are often found in the urine. This result of the presence of biliary matter and perhaps other toxic material in the blood usually vanishes with the disappearance of the jaundice, although rarely a genuine degenerative or inflammatory lesion of the kidney persists.

Long continuance of *gout* usually leads to more or less marked cardiovascular and renal sclerosis, presumably from the influence upon the

<sup>1</sup> *Arch. Inter. Med.*, 1913, xii, 49.

<sup>2</sup> Cf. Fry and Martin, *Archives of Pediatrics*, 1904, xxi, 19.

heart, vessels, and kidneys of the chemical substances present as the result of faulty metabolism. In *diabetes*, also, chronic nephritis is occasionally seen. Here the nephritis is apparently toxic, although the influence of excessive quantities of food, with unusual demands on the kidney in the way of elimination, may play a part. Obesity at times leads to sclerosis of the vessels, and contracted kidney may be found in the fleshy, especially, it would seem, in fleshy women.

It is in place here to refer to the observations of some who have found that when injured renal tissue has been left in the body, as when the kidney is left *in situ* after ligation of the ureter or the renal vessels, the cells of the remaining kidney may undergo degenerative changes, believed to be due to the nephrotoxins (isonephrotoxins) developed from the absorption of the damaged renal tissue.<sup>1</sup> This has been thought to explain in part the progressive character of some cases of nephritis. Others, *e. g.*, Pearce,<sup>2</sup> while able to induce nephritis by using heteronephrolins, have been unable to get positive results with isonephrotoxins.

Martin Fischer<sup>3</sup> has advanced the hypothesis, supporting it by experimental and clinical studies, that the fundamental pathological change in nephritis is an acid condition of the parenchymal cells of the kidney. These cells, he says, represent a colloid membrane interposed between the blood on the one hand and the urine on the other. If the contents of these cells become acid—as through the operation of any of the causes already enumerated—the colloidal albumin becomes “soluble” and appears in the urine. This same acidity explains the casts and the other urinary changes of nephritis, as well as the histological findings in the diseased kidney. In spite of sweeping generalizations often unwarranted by the experimental or clinical data, and though his attractive simplification of the conception of nephritis hardly takes due cognizance of the complexity of the facts of nephritis, especially of the chronic forms, Fischer’s work should be followed up. The physicochemical and colloid explanations of many of the phenomena of nephritis are in many respects far more satisfying and rational than some of the others. Some of Fischer’s experiments are as striking in their simplicity as they are startling in their results. They should be repeated and broadened, for they are concerned with the basic principles underlying such conditions as albuminuria, casts, the occurrence of œdema, etc.

3. **Cold.**—Cold is, perhaps, as Bartels<sup>4</sup> called it, an etiological scapegoat as regards nephritis. Clinical evidence is strong that at times exposure to cold precipitates an attack of acute nephritis or aggravates an already existing chronic nephritis. Just as in tonsillitis or pneumonia cold may favor the activity of pathogenic bacteria, so in the case of the kidney we may look upon cold as favoring the action of infectious or toxic agents that thus produce nephritis. How the cold works in these cases is not always clear. Changeable climate seems to favor the development of nephritis. Eichhorst saw relatively more cases on the East Prussian

<sup>1</sup> Cf. Isobe, *Mill a. d. Grenzgeb. d. Med. u. Chir.*, 1913, xxvi, 1.

<sup>2</sup> *University of Pennsylvania Medical Bulletin*, 1903, xvi, 217.

<sup>3</sup> *Nephritis*, John Wiley & Son, 1912.

<sup>4</sup> *Ziemssen’s Encyclop. dia*, American edition, xv, 254.



Coast than in the more equable climate of Jena and Berlin. Similar observations are recorded by Saundby and by Frerichs.

4. **Pregnancy.**—Pregnancy has been recognized as a cause of nephritis since Rayer first called attention to the fact. There are certainly two conditions that have to be here considered. In the first place, some of the cases of nephritis complicating pregnancy are cases in which a previously existing, but unrecognized, nephritis has been aroused to fresh activity through pregnancy, which may be looked upon, therefore, as merely aggravating the condition. But in the second group are the cases in which kidneys previously healthy are injured during pregnancy, as shown by anatomical study as well as by urinary findings and the clinical symptoms of eclampsia. The cause of this disease of the kidney is still not clear. Rayer and others emphasized the importance of increased intra-abdominal pressure due to the pregnant uterus, and particularly direct pressure upon the vessels of the kidney or upon the ureter.

Toxemia, however, undoubtedly plays an important part, as Virchow insisted. Pregnant women are often, through false notions of modesty, through fear, or because of indisposition, confined to the house, taking insufficient exercise and neglecting even the customary care of the skin. They are often obstinately constipated. Elimination is, therefore, deficient and toxemia favored. Besides, extra demands are made upon the mother in the way of supplying nourishment and elimination for the developing fetus. Metabolic processes, while active, may be perverted, and toxemia result. Perversion of protein metabolism may have much to do with this toxemia.

5. **Predisposing and Contributing Causes.—Heredity.**—There can be no question that a tendency to nephritis is at times transmitted. This is often an hereditary arteriosclerotic tendency, the kidney sharing in the general vascular change. The chronic forms may appear even in childhood. In one family observed by the writer there is a history of renal trouble in the parents and several of the uncles and aunts; one woman of fifty has chronic interstitial nephritis, and her three daughters and one son have had albuminuria from the age of twenty, at least, and cardiovascular changes are already in evidence.

**Age.**—The young are more liable to have the parenchymatous forms, because of their greater liability to infectious diseases. The so-called interstitial forms are oftener seen later in life.

**Sex.**—From greater exposure, severer physical work, and greater carelessness in the matter of food and drink, the male sex will show a larger percentage of cases of Bright's disease, although the influence of pregnancy and pelvic infections goes a long way toward increasing the percentage of cases in women.

**Occupation** may predispose to nephritis. Workers in lead or mercury, those helping about breweries or saloons, where alcohol is often taken freely, are especially prone to disease of the kidney. Engineers, workers in the cooling-rooms of packing-houses, and others engaged in occupations that expose them to extremes of heat and cold are peculiarly liable to the development of parenchymatous nephritis. The modern strenuous

business life with its nerve strain and hustle seems to favor early renal and cardiovascular sclerosis.

**Other Diseases.**—Diseases producing congestion of the kidney, *e. g.*, uncompensated disease of the heart, favor the development of nephritis. Acute nephritis may lead to the chronic form. And, as has been already mentioned, the infections often lead directly to Bright's disease, but probably at times indirectly, the debilitated condition of the patient favoring the action of any accidentally operating cause that might produce nephritis, but which, acting in an individual who was healthy, would be without harmful result.

### ACUTE NEPHRITIS

**Etiology.**—The ordinary causes—acute infections, intoxications, cold, pregnancy, etc.—have just been considered and need not be repeated.

**Pathology.**—In acute nephritis both kidneys are involved, and usually equally involved. Exceptional cases of unilateral nephritis are recorded.<sup>1</sup> The kidney may be of normal size and show few or even no changes that can be detected by the naked eye. Ordinarily, however, it is somewhat larger than normal, and the weight may be twice that of an average kidney. The tense kidney may bulge through an incision in the capsule like a hernia (Dieulafoy). The capsule strips readily. The color varies, depending largely on the amount of blood in the vessels, the hemorrhages and the fatty changes that have taken place; it is usually grayish red or quite dark red, the stellate veins often showing plainly. The kidney usually feels rather soft. On section, the cortex is seen to be swollen, its grayish-yellow or lighter red color showing in sharp contrast to the deeply brownish-red pyramids. The cortex may show yellowish areas or streaks marking the degenerated tubular epithelium, with reddish lines representing the engorged vessels, or reddish dots due to the prominent glomeruli or to smaller or larger hemorrhages.

Attempts to distinguish definitely between the purely degenerative and the more strictly inflammatory changes in these kidneys are only rarely successful. There are certain anatomical peculiarities of the kidney of nephritis, characteristic of different operating causes. For instance, the lesions of scarlatinal nephritis are largely glomerular; in diphtheria the tubular epithelium first shows degenerative changes, especially in Henle's loop; in cholera the epithelium of the convoluted tubes is particularly involved. Similarly in experimental nephritis<sup>2</sup> a selective action of the toxin employed is often seen. Thus, of chemical substances chromium salts and uranium nitrate induce a tubular nephritis, cantharidin affects chiefly the glomeruli, while vinylamin leads to necrosis of the medullary portions with inflammation of the renal

<sup>1</sup> Riesman and Miller, *Arch. Int. Med.*, 1913, xi.

<sup>2</sup> H. A. Christian reviewed the literature on experimental nephritis in the *Boston Med. and Surg. Jour.*, 1908, clviii, 416, 462. He and his co-workers have since then published several valuable studies on this subject; the latest is Study XIX in *Jour. Exper. Med.* References to the other studies are here found.

pelvis, sparing the cortex. With uranium nitrate, as shown by Richter,<sup>1</sup> human nephritis is imitated as to dropsy. The description of the anatomy of the kidney of acute nephritis here given will be that of what may be called the typical acute nephritis, or, if one please, the "average" kidney of acute nephritis, as seen at autopsy.

**The Malpighian Bodies.**—Very often some seem absolutely normal, while others, even those in their immediate vicinity, may show extensive lesions. This irregular distribution of the pathological process in the kidney is found, as will be seen later, in the other renal structures, and in other forms of Bright's disease, and is the more remarkable when we think that the operating cause is so often a toxin or soluble chemical substance in the blood that must come in contact with all parts of the kidney. In acute nephritis *Bowman's capsular space* contains red and white corpuscles, desquamated epithelial cells in various stages of disintegration, even to the extent of being represented by an amorphous, granular debris, and a fluid variously described as serous, albuminous, an inflammatory product, etc., often coagulated, and at times demonstrably containing fibrin threads. The amount of these substances may be very slight or so great as to compress the capillary tuft into a small space. And the proportion of the different ingredients may vary, in the one case the space being filled with an albuminous fluid or with granular material, in another with red-blood corpuscles, this latter condition constituting one of the striking findings in some cases of hemorrhagic nephritis. In fact, in most instances, renal hematuria is of glomerular origin. The *cells of the capsule* may be normal, although many of them commonly show degeneration, as evidenced by their swollen condition, their granular or hyaline appearance, the presence of fat droplets, and the indistinct or vanished nucleus. Large numbers of cells may have dropped off and be seen in the capsular space. This leaves bare areas in the capsular wall, although the denuded spots may be rapidly covered by newly proliferated cells, efforts at regeneration often being shown by mitotic figures. The crescentic masses, so commonly described in the Malpighian bodies of acute nephritis, are made up, according to some, of masses of these proliferated cells lying between the basement membrane of the capsule and the capillary tuft, while others (Ribbert) regard the masses as made up of desquamated glomerular epithelium.

The capillaries of the *glomerulus*<sup>2</sup> are often tensely filled with blood that may be in thrombus form. Cells of uncertain nature, perhaps leukocytes, are sometimes seen in great numbers within the lumen. A hyaline appearance of the entire tuft is often noted. The cells covering the glomerular vessels have undergone the changes just referred to in connection with the capsule. At times proliferation has been active, and little more can be made out than a compact mass of epithelial cells, with deeply stained nuclei. The hyaline appearance is seen in the kidneys in many acute infections, and involves the capillary wall.

<sup>1</sup> *Beiträge zur klin. Med., Senator Festschrift*, 1904.

<sup>2</sup> Cf. Christian and O'Hara (loc. cit., Study XIX) for excellent figures of these glomerular changes in acute experimental nephritis.



It can readily be understood from a consideration of the glomerular changes just described that the plugging of the capillaries with thrombi, the filling of the capsular space with exudate and debris, with resulting pressure upon the vessels of the tuft and upon the tubules, must result in marked disturbance of glomerular function. In the glomerular lesion is found the main, although not the sole, explanation of the albuminuria, a partial explanation of the oliguria, and perhaps, through the obstruction that is offered to circulation, one of the causes of increase in blood-pressure. Moreover, the circulatory disturbance in the capillaries of the glomerulus must contribute to the nutritional and functional disturbance of the tubular epithelium.

**The Tubules.**—The same irregularly distributed or patchy arrangement of the diseased areas that was noted in the case of the Malpighian bodies is seen in the tubules. The cells are swollen, hazy or granular in appearance, the nuclei indistinct or invisible. In other cells the nuclei may still remain, but the brush-like appearance of the cell has disappeared, and it looks hazy or hyaline. Fat droplets are frequently seen. The lumen of the tubule may be perceptibly narrowed by the swelling of its cells, although, at times, the lumen is increased because the cells are flattened or more or less disintegrated and their places taken by fragmentary relics, or they have entirely disappeared or are seen not in their proper places but in the tubules. Regenerative appearances are occasionally described. Red- and white-blood corpuscles are also seen in greater or less abundance, and casts of different kinds. In some instances the lesions in the kidney are confined to the tubules, constituting the so-called tubular nephritis.

**The Interstitial Tissue.**—Usually, even in some of the more recent cases, an inflammatory oedema is shown by the widening of the intertubular spaces. Round-cell infiltration may occur, especially in the neighborhood of the glomeruli. Hemorrhagic areas are not unusual. The vessels show varying degrees of engorgement. In cases of longer standing, such as perhaps might be termed subacute, proliferative changes in the connective tissue may be detected. This is sometimes well seen in a slight thickening of Bowman's capsule. The term parenchymatous as commonly applied is in reality a misnomer, for in nearly every case of acute nephritis definite interstitial lesions can be made out.

In some instances, especially of acute infections, the striking change is seen in the interstitial tissue, which may be the seat of an inflammatory oedema, but whose chief feature is the presence, sometimes focally, or again more diffusely, of larger or smaller numbers of cells that have been variously described by different writers, but which have been shown by Councilman<sup>1</sup> to consist in large measure of cells identical with Unna's plasma cells. Degenerative changes in the epithelium of the tubules and glomerular changes may be slight or marked in this form of "acute interstitial nephritis," so that albuminuria and other ordinary urinary evidences of Bright's disease may be quite variable as to degree. The

<sup>1</sup> *Transactions of the Association of American Physicians*, 1898, xiii, 300.

so-called "lymphomatous nephritis" is of a somewhat similar nature, and is seen, for example, in the kidneys of typhoid fever.

The changes in *organs other than the kidney* are often those of the primary disease, *e. g.*, an acute infection. Dropsical conditions may be found, or there may be lesions of some complicating affection such as pericarditis or pleuritis. In cases of acute nephritis lasting over a few weeks hypertrophy of the left ventricle can sometimes be made out. Henschen<sup>1</sup> and his pupils have shown this to be true in a number of instances.

**Symptoms.**—From the clinical point of view there are two types of acute nephritis. The one is characterized by an abrupt, frank onset, with œdema, pallor, headache, and gastric disturbance, and by such scantiness of urine and change in color from admixture of blood as commonly to attract the attention even of the patient or the nurse to the fact that there is something wrong. The second type is less frank in its manifestations. Although the onset may be sudden there is no marked œdema or pallor of the skin, there is no complaint of headache, no nausea or vomiting, and the urinary change is only revealed by a close watching of the amount of urine and by its chemical and microscopic study. Scarlatinal nephritis may serve as typical of the first class; the acute nephritis occurring during the course of typhoid fever or pneumonia is fairly typical of the second class.

The *frank form*, as has been said, is the one met with in scarlet fever. In many of the acute infectious diseases, especially when accompanied by high fever, a trace of albumin with a few casts can frequently be found in the urine. This is true of scarlet fever. As the fever subsides the casts and albumin disappear and the urine is practically normal. This is the so-called febrile albuminuria. The true scarlatinal nephritis is more apt to occur during convalescence. In some cases there has been no relaxation of the vigilant care on the part of nurse or physician; the patient is still in bed, still on restricted diet, and an apparently favorable convalescence is rudely interrupted by the renal disease. Although it is, perhaps, more apt to appear following the severer attacks of scarlet fever, it is not infrequently seen after mild, even ambulatory, cases.

While there are many deviations from the type, as here described, it may be said that the three striking features, at least the three features that are most prominent early in the disease, are œdema, uremic manifestations—especially headache, drowsiness, and disturbance of the stomach—and the marked change in the urine.

The *œdema* may come on with remarkable rapidity. The child's face in the morning may be seen to be puffy, the eyelids swollen, these appearances, with the obliteration of the wrinkles, the pallid, pasty color, and the watery eye, causing a peculiar apathetic, expressionless look that is quite characteristic. The same œdematous condition may be found on the back of the hands, over the lumbar vertebræ and sacrum, constituting the "lumbar pad," and in the loose scrotal tissue. The œdema at first may be rather firm and does not pit readily. This œdema may never

<sup>1</sup> *Das Herz bei Nephritis*, Jena, 1898.

become extreme, although in some instances it progresses and dropsical accumulations are found not only in all the subcutaneous tissues but in the peritoneal, pericardial, and pleural cavities as well.

While dropsy in acute scarlatinal nephritis is usually quite general, it is sometimes capriciously fugitive, shifting for no assignable reason from one part of the body to another. It will often show a tendency to shift with the position of the patient, and be most marked in the dependent portions of the body. In patients in bed it can often be detected over the lower back, when not noticeable in the extremities. In certain rare instances the fluid collects in the serous cavities to a much more marked degree than in the subcutaneous cellular tissue. Cases of œdema without albuminuria, following scarlet fever, are occasionally seen. They were early described by Hamilton, Phillipp, Goodak, Henoch, Bartels, and later by several others, but the correctness of the observations of Phillipp<sup>1</sup> of a remarkable series of sixty such cases may be justly questioned. One such case has come under personal observation. Most of these cases resemble nephritis in all respects, although without the ordinary urinary accompaniments. Albumin and casts, in some instances, have appeared later. Autopsies in some have shown an underlying condition of nephritis.<sup>2</sup> Edema may exceptionally appear before albumin; casts (Rosenstein) and blood (Mahomed) may precede the albumin, while in other cases albumin may be present many days before œdema is noticeable.

This fluid interferes more or less with the functions of various organs, *e. g.*, of the stomach and intestine, whose walls may be œdematous, or of the lungs, as when the abdominal and pleural cavities contain much of the transudate and the free play of the lungs is interfered with by the pressure of the surrounding fluid. Edema of the glottis, fortunately comparatively rare, may be serious or even fatal. Edema of the uvula may be annoying and extremely alarming to the patient. Some of the cerebral symptoms, such as headache and apathy, may be in part explained by cerebral œdema.

The *urine* is scanty. A few ounces only may be passed in twenty-four hours, and complete suppression may occur. There may, however, be a frequent desire to urinate and a somewhat painful vesical tenesmus may be present, only a few drops being squeezed out with each effort. Suppression may continue for many hours, and yet recovery be possible. The writer has known anuria to last sixty hours, in the case of a child who ultimately recovered. Rosenstein saw anuria of three days, Riegel of ten. The urine that is passed is turbid, smoky, reddish, brownish, or flesh-colored, usually acid, and deposits a heavy sediment. If the urine be alkaline, a relatively small amount of blood gives it a bright red color (Tyson). The specific gravity of the concentrated urine is at first high, often over 1.020 or even 1.030. There are, however, many exceptions to this rule. Albumin is present in large amount, even to 1 per cent., or, in rare instances, more. The daily loss seldom exceeds 20 grams, although Dickinson sets 35 grams as the limit. The percentage of solids, urea,

<sup>1</sup> Cited by Frerichs.

<sup>2</sup> Cf. Henoch, *Berl. klin. Woch.*, 1873, No. 50.



chlorides, phosphates, is increased, although the total output for twenty-four hours, owing to the scantiness of the urine, is less than normal. Bartels noted, what has lately attracted much attention in connection with the dechloridation treatment of nephritis, that the chlorides were diminished, especially in cases attended by dropsy. Accurate clinical observation is needed along the lines laid down by Schlayer and Takayasu<sup>1</sup> who found striking differences in the elimination of different solids to depend upon the portion of the kidney affected in experimentally induced nephritis. Thus extensive tubular damage interfered with the elimination of sodium chloride and potassium iodide; lactose elimination, however, was affected by vascular damage.

The microscope shows that the sediment is made up largely of red blood corpuscles, epithelium, casts, uric acid crystals, and amorphous urates. The red cells may be well preserved or broken down into a reddish-brown, granular detritus. Shadow corpuscles are numerous. White corpuscles and, as Senator has shown, many of the mononuclear type are seen. Epithelial cells are abundant and casts of various kinds are found. At first blood casts and epithelial casts are especially numerous, but soon hyaline and granular forms are seen, and fatty casts, as well as waxy casts, may be met. No one form can be regarded as characteristic of an acute inflammation. While casts in the albuminous urine of acute nephritis may perhaps be lacking in rare instances, care should be exercised in making such a statement, for often the absence of casts is to be explained by the early decomposition of the urine, especially if collected in an unclean receptacle in hot weather. The destructive digestive action upon casts of alkaline urine, and particularly of alkaline urine full of bacteria, should be remembered before one declares that the urine of a patient is free from casts. Cases without casts are, however, occasionally recorded, as by Dickinson.

The molecular concentration of the urine is increased, as is its electric conductivity. The freezing-point is, therefore, lower than normal. The freezing-point of the urine, however, is subject to wide variations. There is retention of solids, *e. g.*, urea, phosphates, and chlorides, and this retention, especially of salts like the chlorides, should bring the freezing-point nearer 0° C., as it sometimes does. But there may be such concentration of the urine, owing to deficiency of water, that the freezing-point may be lower than normal, *i. e.*, it may be below -2.3° C. A frequent phenomenon in disease of the kidney is the inability to pass a concentrated urine. The passage of an abnormally dilute urine occurs, constituting the hyposthenuria of Friedrich Müller.<sup>2</sup> Hyposthenuria is seen not alone in chronic interstitial nephritis but also in acuter forms, especially when there is glomerular involvement, as in the form under consideration. Unless hyposthenuria be counteracted by polyuria, renal insufficiency must result. This condition is often seen early in acute nephritis, and although the urine is diminished in amount, yet it may contain but a small amount of solids, be of low specific gravity,

<sup>1</sup> *Deut. Arch. f. klin. Med.*, 1910, xcviii, 17.

<sup>2</sup> *Loc. cit.*, p. 71. Cf. also, for a discussion of hyposthenuria and polyuria in acute experimental nephritis, the article cited by Schlayer and Takayasu.

and have a freezing-point nearly that of the blood. Slow and deficient elimination will be shown by the phenolsulphonephthalein test.

After what may be called the initial shock of the disease, the urine becomes somewhat more abundant, less dark and smoky in color, its percentage of albumin less, and the casts more varied in their character. One of the earliest signs of recovery is an increased output of urine. Especially if œdema has been extreme and there is a rapid subsidence of it, the amount of urine as convalescence is established may be excessive and the specific gravity as low as 1.010 or 1.005. Dickinson reports having seen 240 ounces in twenty-four hours. The albumin and casts gradually disappear, although spasmodic outbursts of albuminuria and cylindruria may be noted, often for weeks. Eriberg,<sup>1</sup> discussing this postnephritic albuminuria as seen in children, is inclined to regard it as generally benignant and not necessarily an indication of a beginning chronic nephritis. Red-blood corpuscles may be found at times long after the albumin has finally disappeared (Rosenstein).

Many of the symptoms that are now to be described are clearly of toxic, *i. e.*, *uremic* origin. *Nausea* and *vomiting* are fairly common symptoms. They are at times so nearly coincident with the retention of urine and the albuminuria as to make one think of the existence of a toxin producing at the same time the lesion in the kidney and the disturbance of the stomach, perhaps through its nervous mechanism rather than a retention toxemia through faulty elimination attending urinary suppression. In other cases—in most cases—there is a rather close relation between the amount of urine secreted and the severity of the gastric disturbance. Within the first few days, when perhaps less than five or six ounces are passed, there is complete anorexia, nausea, and prompt rejection of food, drink, or medicine that may be put into the stomach. The tongue becomes coated and dry; stomatitis and gingivitis resembling that of scurvy have been described. There is a fetid odor to the breath, at times suggestive of urine. This urinous odor may be detected in the vomitus. The bowels may be constipated or loose, diarrhœa being oftener a late than an early manifestation. Vicarious elimination through the stomach and bowel is regarded by many as an explanation of the vomiting and the diarrhœa.

There is rarely much *fever*. Occasionally an initial chill or chilliness will be followed by quite a sharp rise to 102°, or even more. Oftener the temperature even at the onset will be less than 100°, or even normal. It is not correct, however, to regard acute nephritis as an afebrile disease, for, in many cases, careful observations will show a slight rise. The fever rarely lasts more than a few days, unless inflammatory complications or uremic convulsions with coma occur. Leube<sup>2</sup> saw no case of nephritis with fever during an entire decade, and then saw several in succession that were febrile.

The *pulse* increases in rapidity and often even quite early has a hard, high-tension quality, showing a rise in blood-pressure. In other cases a slow pulse may be present. In fact, some regard bradycardia

<sup>1</sup> *Nord. Med. Arkiv*, 1911, Abt. ii.

<sup>2</sup> *Diagnostik der inneren Krankheiten*, 1895, i, 322

as quite characteristic of acute nephritis. Often even by the end of a month a definite enlargement of the *left ventricle* can be made out, and with the loudness of the first apical tone and the sharpness of the aortic second, make it clear that the vascular tension is high, a fact readily confirmed by the sphygmomanometer. Dilatation may occur at any time. These cardiovascular changes, however, are not to be detected in all cases, although a sharp aortic closure is common. As convalescence ensues, the pulse may become quite slow and intermittent or even irregular. Permanent cardiac derangement after acute nephritis is rare, unless infectious cardiac complications have occurred. Occasionally one sees a moderately hypertrophied heart in adult life, when from the history one would suspect an acute nephritic origin.

The *skin* is dry and if œdema is excessive may be glossy and look unnaturally thin and transparent. Pruritus may lead to scratching and infection. Papular and erythematous eruptions sometimes occur, presumably to be classed under the head of the toxic dermatoses. A few times with uremia a white frost-like deposit of urea has appeared on the skin.

The *blood* is that of secondary anemia, the reduction in hemoglobin being more marked than that of the red corpuscles. The pallid, pasty appearance of acute nephritis is due in part to a genuine loss in erythrocytes and hemoglobin, and also to a thinning of the blood in the vessels due to hydremia, and to the spreading out of the capillary vessels over an increased area, caused by the œdematous swelling. The molecular concentration tends to be increased, but there are great modifications of this rule. An increase of œdema or of anemia generally lessens the molecular concentration of the blood, and the freezing-point under these circumstances may be normal,  $-0.54^{\circ}$  C. or even less than this, *e. g.*,  $-0.56^{\circ}$  C.

Hemorrhages are relatively rare in acute nephritis, although nosebleed is sometimes seen and occasionally hemorrhages in the retina are noted. In the cases with purpuric manifestations, the renal condition appears to be secondary, the purpuric lesions or the erythematous nodes distinctly antedating the albuminuria.

*Respiratory symptoms* are usually due to a bronchitis or to œdema of the lungs and bronchi. Œdema of the lungs in nephritis is, however, quite often cardiac in its origin, although primarily to be ascribed to the kidney. The combination of bronchitis and pulmonary œdema may result in what has been termed "serous pneumonia." True lobar pneumonia is rare as a complication, bronchopneumonia somewhat more frequent. Dyspnœa may be uremic or cardiac in origin, due to the extensive bronchitis and œdema, or may be caused by the pressure of accumulations of fluid in the pericardial, pleural or peritoneal sacs. True intercurrent pleurisy is not so very rare. Cheyne-Stokes breathing is often a manifestation of uremia. Attacks of dyspnœa are apparently at times uremic or at times cardiac in character.

*Headache* is frequently an early evidence of nephritis. As uremic intoxication becomes more pronounced, it may be a most distressing, almost unbearable, condition. Dizziness and tinnitus may be other



manifestations. Not a few patients grow apathetic, drowsy, even stuporous or comatose, without convulsions. The mind may be clouded and delirium of a low and muttering type or of a wilder character may manifest itself. *Amaurosis*, palsies and uremic deafness and retinitis are rare as compared to their frequency in chronic interstitial nephritis.

*Convulsions* rarely occur until the nephritis has lasted for several days or weeks. They are of the epileptiform character, and are usually preceded and in a sense heralded by severe headache, vomiting, epigastric pain, with increase in pulse tension, and perhaps muscular twitchings. Coma may follow the attack, and is particularly apt to supervene on several attacks that follow one another in rapid succession. In some cases the torpor and drowsiness may pass into a coma, perhaps fatal, without there being any convulsion. These cases are more often those in which an early nearly complete suppression of urine has occurred. They resemble in some respects the toxemia of anuria as seen in cases of several weeks' standing<sup>1</sup> rather than that of true uremia.

General *malaise*, with more or less aching in the limbs, is apt to be present, particularly when there is much fever at the beginning. There is often pain in the back, of a dull aching character. At times it may be severe enough to justify Basham's description of an "urgent aching pain across the loins." Rayer's observation that he had never in acute nephritis seen a retraction of the testicle or the radiation of pain along the ureters has been generally confirmed. Even the passage of blood in the shape of clots is so rare that pain from this cause partaking of the character of ureteral colicky pain is almost never noticed. There may be some tenderness on pressure in the loins over the region of the kidney. Vesical tenesmus with some slight urethral burning during micturition may be annoying, but is seldom very painful. Concentration of the urine may explain in part the frequent and burning micturition. There is sometimes complaint of pain in the epigastrium, aside from the discomfort attending the nausea and vomiting.

*Nephritis from Cold; Nephritis à Frigore.*—While one can hardly agree with Rayer or Stewart when they say that the most common cause of inflammation of the kidney is exposure to cold and wet, one must admit that at times a very definite influence of cold is seen in producing acute Bright's disease. Lassar's experiments on lower animals seem to show the positive influence of cold in this direction. It is apparently not so much cold alone as prolonged or repeated exposure to cold and wet, coupled with exhaustion, starvation, and the excessive use of alcohol.

Clinically, nephritis of this type resembles very closely the type seen in scarlet fever. The onset is usually abrupt, the œdema frankly generalized and the urine rich in albumin, casts, and blood. Chilliness, with some rise of temperature, may be present, and there is a dull pain in the loins. Uremic headache, apathy, nausea, convulsions, or coma may or may not be pronounced. Some of the cases are more insidious in onset, and in their long-drawn-out course might be classed as subacute

<sup>1</sup> For a good discussion of the differences between uremic and anuric intoxication phenomena, see Ascoli, *Die Uraemie*, 1903, p. 144, et seq.

or even be said to merge imperceptibly into the chronic parenchymatous form. Recovery from acute nephritis due to cold is the rule, although it is often a matter of many weeks or even months. Bartels saw a recovery after a duration of one year.

*Alcoholic excess* is a factor in the production of both acute and chronic nephritis. Strümpell describes cases as occurring in the heavy beer drinkers of Bavaria, particularly in the obese and after exposure to cold. The œdema in these cases was pronounced, and made its appearance rapidly; the urine was scanty and heavily albuminous, while casts were plentiful; blood was absent, and the urine was not smoky or even turbid. In the instances in which alcohol appears to be the exciting cause there is commonly a history of a definite, usually prolonged period of excessive drinking rather than of habitual indulgence; or some debilitating condition, such as tuberculosis, heart disease, or anemia, has already been present. The onset is often rather insidious than outspokenly active, and the course of the disease borders on the subacute or chronic parenchymatous, the cardiovascular changes not being a striking feature. Many of the cases of excessive albuminuria and cylindruria accompanying acute alcoholism seen by the writer have been, as shown by the subsequent history, acute exacerbations of a chronic nephritis rather than a true primary acute inflammation.

In many of the *infectious diseases*, as has been said, there is a form of nephritis differing in its clinical behavior from that met with in scarlet fever. The difference is seen in the more insidious onset, the lack of œdema or its comparatively slow and only slight development, in the absence of pronounced headache, nausea, and vomiting, and in the rarity of marked hematuria and scantiness of urine. In many of these cases, too, the symptoms of nephritis are lost in those of the primary disease that is still at its height, and they do not stand out prominently against the background of symptomless convalescence as in scarlet fever. It is possible that in the future clinical features characteristic of acute nephritis due to different infectious agents will be recognizable. As yet only the composite picture is known. The diagnosis depends almost entirely on the examination of the urine, which should always be made at the beginning of every infectious disease as well as at frequent intervals later. Febrile albuminuria and exacerbations of a chronic nephritis are to be excluded. Absence of œdema by no means rules out nephritis. The possibility that the nephritis is really due to drugs, cold or other infectious organisms than the one involved in the primary illness should also be kept in mind.

In nearly every known *infectious disease* acute nephritis has been observed as a complication. Among these may be mentioned diphtheria, lobar pneumonia, influenza, typhus fever, smallpox, varicella, measles, erysipelas, rheumatic fever, septicemia. The purpuras not infrequently show nephritis, often with œdema. Ulcerative endocarditis, which is really a sepsis, often shows a sharp, virulent, acute nephritis which is sometimes clearly embolic in origin. With pulmonary tuberculosis nephritis of an acute or subacute type, with or without œdema, is not unusual. In the nephritis accompanying tuberculosis the heart is

normal in nearly all cases.<sup>1</sup> The relation of syphilis to nephritis has already been discussed. In malarial nephritis œdema is common and it may be present in the influenzal form.

By this form of acute nephritis is meant something different from the so-called *febrile albuminuria* that is so commonly seen in most acute infections. This trace of albumin with an occasional cast or red-blood corpuscle is without accompanying clinical symptoms that can rightly be ascribed to renal change. While some anatomists regard the acute degeneration causing this as inflammatory, a sharp line must be drawn between this condition, coincident with the fever, and the nephritic form that may occur either at a time when the fever is present or has passed. This latter form is accompanied by symptoms due to defective renal function, and by characteristic urinary findings; its existence usually long outlasts the duration of the primary specific infectious disease.

In *typhoid fever*, acute nephritis may be an early occurrence, constituting the so-called *renal typhoid*. More commonly it occurs during the height of the fever or just as convalescence seems in sight. There is rarely any appreciable increase in temperature, complaint of pain on the part of the patient, or œdema. It is only by the frequent routine examination of the urine that the existence of the complication is recognized. Albumin and casts are abundant; blood is present in varying quantities. These urinary findings may last for from several days to many months. In such cases the outlook for recovery is generally fairly good, although there is not only the original disease but the added danger of uremia and such complications as pneumonia or serositis.

In *Asiatic cholera* there is oliguria. In severer cases there is anuria which may last for hours or days. What urine is passed is concentrated and contains an abundance of renal epithelial cells in various stages of degeneration, and often some albumin and a few casts. In some cases of cholera the urine is heavily albuminous and contains large numbers of casts, red-blood corpuscles, epithelial cells and debris. Indican and diacetic acid may be present. This form of nephritis is believed to be a strong contributory factor in the causation of the headache, convulsions, coma, and death that often follow at the end of a few days. Dropsy is rare. Recovery after anuria of seven days is exceptional.

Bamberger, Litten, Aufrecht, and others have described a *primary acute nephritis*. Strümpell also refers to it. It is frank in onset, with chilliness, some fever, pain in the back or in the extremities, headache, nausea, and œdema. The spleen is said at times to be enlarged. The urine is scanty and contains albumin, casts, and blood. After days or weeks recovery usually ensues, although occasionally death or a chronic form of nephritis results. For this so-called primary or idiopathic nephritis no cause is discoverable. Presumably some unrecognized infection or intoxication will explain the majority of the cases.

**The Kidney of Pregnancy.**—During pregnancy renal changes are often met with that are accompanied, as a rule, by abnormal urinary findings,

<sup>1</sup> Walsh, in *Third Annual Report of the Henry Phipps Institute*, 1905-06, p. 357. Senator and Müller find the same lack of cardiac hypertrophy.



and at times by recognizable clinical symptoms. These lesions of the kidney, because of certain anatomical peculiarities, of the uncertainty as to their inflammatory nature, and because of the atypical accompanying clinical manifestations, are not generally classed as nephritic. The tendency to-day is to speak of this kidney as the "kidney of pregnancy." It is to be remembered that an already existing, although previously unsuspected, nephritis is liable to become aggravated under the influence of pregnancy. These instances of true nephritis with or without uremia are not to be classed with the so-called kidney of pregnancy.

The explanations offered for the origin of the kidney of pregnancy are varied and in a measure largely speculative. They may be conveniently classed as (a) bacterial; (b) mechanical, *i. e.*, pressure; (c) toxic; (d) a combination of these three causes.

No proof that bacteria play the primary rôle has been advanced. Pressure upon the ureter, renal vessels or even the kidney<sup>1</sup> itself during pregnancy or even, as Webster<sup>2</sup> suggests, by the plugging of the pelvic opening for two or three days postpartum by the still large uterus, may explain certain renal changes. But the toxic theory first brought prominently forward by Virchow,<sup>3</sup> in 1848, is worthy of the greater consideration. The present view is, however, that the toxemia is general, not essentially renal. Thrombotic, hemorrhagic and necrotic lesions in the liver may be as characteristic as the degenerative changes in the kidney. Puerperal eclampsia has been seen without renal disease. The toxin is unknown. It results in faulty protein metabolism.

The clinical manifestations vary from a trace of albumin with a few casts in the urine, but no subjective symptoms of toxemia—a condition that is regarded by many as rather physiological than pathological, especially in the last weeks of pregnancy—to a heavily albuminous urine, containing casts and blood, and subjective symptoms suggestive of most profound toxemia, and culminating oftentimes in an eclamptic explosion. The urine, when this condition is at all advanced, is usually somewhat scanty, turbid, the specific gravity averaging higher than normal. Albumin is present and may be excessive in amount. Casts generally of the hyaline or granular varieties are present, as well as some red-blood corpuscles, a few leukocytes, and renal epithelium in various stages of degeneration. Ammonia is often high, the urea low, a point of some value in differentiating from a true nephritis.

Edema is common not only in the dependent portions of the body, as the legs, where pressure on the return circulation might in a measure account for it, but in the face, the hands, the back. Sometimes a pallor gives the patient the pasty look seen in typical cases of parenchymatous nephritis. Symptoms of toxemia are more or less pronounced and resemble those commonly described as uremic. Among these may be mentioned headache, dizziness, sleeplessness, apathy, dimness of vision amounting at times to amaurosis, nausea and vomiting, epigastric uneasiness or even severe pain, unusual dyspnoea, perhaps diarrhoea

<sup>1</sup> Halbertsma, *Centrabl. f. d. med. Wissenschaft*, 1871, No. 27.

<sup>2</sup> *Text-book of Obstetrics*, p. 314.

<sup>3</sup> *Gesamte Abhandlungen*, 1856, p. 778.

or obstinate constipation. These may be the forerunners of an epileptiform seizure, occurring in the later months of pregnancy, during labor, or in the first few days thereafter. If the attack passes away, recovery may ensue promptly, the urine clearing rapidly.

The *diagnosis* of the kidney of pregnancy is usually a simple matter if the physician has knowledge of the condition of the urine at the beginning of pregnancy. Otherwise, he must consider whether he is dealing with a renal congestion, a chronic nephritis with the added element of congestion, or an acute nephritis. A positive diagnosis is at times impossible. Simple congestion rarely gives the large amount of albumin found in the urine of the kidney of pregnancy, nor does it cause the generalized cedema or the marked toxic symptoms of that condition. Of great help in the diagnosis of an old nephritis is the finding of typical cardiovascular changes or albuminuric retinitis, as well as a history of polyuria before pregnancy. It may be impossible to differentiate acute nephritis from the kidney of pregnancy, although especially liable to have more blood and more casts and to be attributable to some acute infectious process. The urine in either the acute or chronic nephritis will not, of course, clear up as promptly on emptying the uterus, as in the case of the kidney of pregnancy, nor do the toxic symptoms subside as rapidly. The *prognosis*, except when eclampsia occurs, is not serious. If eclampsia occurs, the mortality of the mother is about 25 per cent.; for the child still greater.

The *treatment* of the kidney of pregnancy and the nature and treatment of puerperal eclampsia are matters for discussion in a text-book on obstetrics, yet a brief word may be here said on the subject of therapy. Too great caution cannot be observed in watching for the appearance of albumin and casts in the urine of the pregnant woman, and for the occurrence of cedema of the face and hands, headache, unusual dizziness, blindness, epigastric pain, etc. These things should be viewed with suspicion, as possibly indicating the existence of the kidney of pregnancy with impending eclampsia. Special care should be exercised in the case of the woman who may have had eclampsia in some previous pregnancy. It is to be remembered, too, that eclamptic seizures have occurred in the non-albuminuric pregnant woman, so that the toxemic symptoms should be regarded as notes of warning. For the eclampsia, sedatives, such as bromides, chloral, and chloroform, should be employed; bleeding may be of benefit, and saline infusions may help to dilute and wash out the toxin. Fischer's<sup>1</sup> treatment by hypertonic solution of sodium chloride and sodium carbonate may here be of benefit; 1000 cc. of water containing 15 grams of sodium chloride and 20 grams of crystallized sodium carbonate are injected intravenously; the solution may be given per rectum. The uterus should be promptly emptied.

In general, the treatment of the kidney of pregnancy is that of acute nephritis; the same hygienic and dietetic precautions, the avoidance of overexertion, a goodly amount of rest, daily warm baths, and as free elimination as possible through the bowel, skin, and kidney.

<sup>1</sup> Fischer, *loc. cit.*

**Complications.**—Among these must be mentioned bronchitis, which may lead to a bronchopneumonia. True croupous pneumonia is not so very uncommon, and its course is apt to be rapid. It may be readily overlooked, unless careful physical examination be made, for bronchial cough, dyspnoea from uremia or from cardiac causes, or perhaps from hydrothorax, may obscure symptoms by offering a plausible explanation for respiratory manifestations otherwise quickly attracting attention as possibly indicative of pneumonia. Edema of the chest wall, fluid in the pleural sacs or pericardium, and bronchial râles often make physical exploration for pneumonic consolidation quite difficult. The upper lobe is said to be very frequently the one involved in acute nephritis. By some a form regarded as a “lobar non-croupous pneumonia,” a serous pneumonia (Fürbringer), is to be distinguished from the ordinary complicating croupous pneumonia. While one is seldom in doubt as to which disease is the primary one, occasionally when the early history of the case is lacking, as often happens in hospital practice, the question as to whether a pneumonia has given rise to an acute nephritis or the nephritis has been complicated by a pneumonia, is not an easy one to decide.

The great frequency with which the pleura, pericardium, and peritoneum show inflammation during acute nephritis is well known. Daily examination is necessary in order to detect these complications, and even slight pain and tenderness should receive careful consideration. Other complications or intercurrent troubles may, of course, occur, such as meningitis or erysipelas. Edema of the glottis is a serious manifestation which might be classed as a complication.

**Diagnosis.**—The diagnosis of acute nephritis presents little difficulty if the physician is familiar with the condition of the patient before the onset of the renal disease; the sudden appearance of the characteristic urinary findings leaves little doubt as to the nature of the trouble. When one has no knowledge of the previous condition of the kidney there may be a question as to diagnosis. Among the conditions most liable to cause confusion are cyclic albuminuria, febrile albuminuria, congestion, acute exacerbation of a chronic nephritis, chronic parenchymatous nephritis, amyloid kidney, infarct, and more rarely such conditions as tuberculosis, tumors, calculus, pyelitis, etc. The main points in the differentiation may be briefly stated as follows:

*Cyclic albuminuria*, or the albuminuria of adolescence, is seen in the young, unaccompanied by oedema, cardiovascular changes, or uremia. The urine shows no blood, only occasionally casts; the albumin is not constant, is usually rather small in amount, and is especially apt to be noted after a heavy meal, after exertion, or after the patient has been on his feet for a time (orthostatic albuminuria).

*Febrile albuminuria* is seen during the acute infections accompanied by fever. The albumin is but a trace; casts and blood are not abundant; there is no oedema or uremia. No increase in blood-pressure that can be attributed to renal disease is made out. There are cases, however, as has been said, in which it is difficult to draw a sharp line between a marked febrile albuminuria and a mild grade of acute nephritis.

In *congestion* of the kidney a cause is seen as in a non-compensated



cardiac disease or other condition lowering arterial pressure. Dyspnœa, congestion of the liver, and œdema of the lower extremities, with other evidences of cardiac incompetence, may show the existence of such a cause. The general anasarca of nephritis involving face, hands, etc., is not present. The urine is concentrated, but contains what for acute nephritis would be a small amount of albumin and a small number of casts. The therapeutic test is often of great value; rest in bed with treatment directed to the cause, *e. g.*, the heart, if successful will result in a prompt return to normal conditions in the urine.

*Chronic parenchymatous nephritis* and the acute form run imperceptibly into each other. Unless we know the definite history from the beginning, showing an abrupt onset, a causal relation to an acute infection or acute intoxication, the early urinary suppression, hematuria, etc., a definite differential diagnosis may be impossible until careful watching and time enable one to determine the chronic character of the disease.

A condition that is very common and one that frequently causes confusion as to diagnosis is a chronic diffuse or interstitial nephritis, on which there is engrafted an acute inflammation. The existence of the chronic trouble may have been unknown to either patient or physician. The acute onset, œdema, headache, nausea, etc., call attention to the kidney, and the urine, richly albuminous and containing numerous casts and blood-corpuscles, resembles that of an acute nephritis. Suspicion as to the previous existence of a chronic disease should be aroused by a history of polyuria—especially nocturnal—headache, dyspnœa, gastric disturbances, etc. When on examination typical cardiovascular changes are found, more marked than could be accounted for by an acute nephritis of only a few days' duration, or when an old albuminuric retinitis is found, there is strong ground for believing that the acute process has been lighted up on the basis of an old affair. It often happens, too, in cases of this kind, that a study of the twenty-four hours' urine will show an amount somewhat above the normal, a specific gravity a little low—say 1.012—while the albumin, blood, and casts are abundant.

**Prognosis and Termination.**—Acute nephritis is always a serious disease. Yet it has a natural tendency toward recovery, and in the great majority of cases—the exact percentage it is impossible to state—a recovery ensues that seems to indicate a complete restoration of function on the part of the kidney, although some are inclined to look upon such a kidney as thereafter peculiarly vulnerable and especially liable to be again involved in a recurring inflammation. Early relapses or, more strictly, exacerbations of the acute nephritis are not so unusual, and should make one guarded in his statements as to outcome until the urinary and other evidences of the disease are well out of the way. The length of time that must ensue before recovery occurs varies greatly. One month is a short time. Yet even after six months, a year, or exceptionally even longer, recovery may take place.

Aside from recovery, a pseudorecovery is occasionally seen, *viz.*, the passage of the acute into the chronic form without œdema. Rayer<sup>1</sup>

<sup>1</sup> *Traité des Maladies des Reins*, 1839, vol. ii, p. 112.

gives a very graphic description of these cases of supposed recovery which lull the unsuspecting patient and the easy-going physician into a false feeling of security, and which in later years show evidence of the long-standing existence of the renal disease that has been overlooked.

Death in acute nephritis may occur in a variety of ways. Uremia is a common cause, with convulsions or coma, or perhaps indirectly through the exhaustion it brings about by loss of sleep, anorexia, vomiting, diarrhoea, anemia, etc. In some instances there is an abrupt, nearly complete or quite complete suppression of urine. This may last for a few days without serious consequences, but unless the urinary elimination be reëstablished, death from anuria follows, and this happens in a certain proportion of cases. The complications already mentioned may be the cause of death. Dickinson says that, while in those over sixteen uremia is the common cause of death, in those under this age in 50 per cent. it is inflammation of the respiratory tract, uremia taking second place. Edema may contribute largely to bring about the fatal result. Cerebral hemorrhage is rare as compared to its frequency in the chronic forms. Occasionally an acute anemia from severe nosebleed, or hemorrhage from the stomach or bowel, will have a decided influence. Cardiac weakness and dilatation, sometimes sudden, may also be fatal. And, as stated, death may be long deferred and occur as the result of the secondary chronic form of the disease.

No definite data as to how to make a prognosis in a given case can be given. Some help may come, at least in predicting uremia, from a cryoscopic study of the urine and blood, as well as from watching for a rise in blood-pressure which often precedes uremia. Various criteria on which to base a prognosis are given by different authors, but in reality one must judge each case on its merits and still feel, even after a careful weighing of all facts, that it is a very difficult and uncertain matter to forecast the future in acute nephritis. Bartels, for example, says that every case with complete suppression is fatal, but exceptions to this occur, as the writer can testify from personal observation. Fürbringer regards the prognosis as especially bad when the urinary sediment is rich in lymph corpuscles. Dickinson thinks the total absence of blood in the urine is not a good sign, as bleeding relieves the organ. He also says that the majority of fatal cases die inside of six months. Other prognostic aids might be cited, but they are quite unreliable.

**Treatment.—Prophylaxis.**—Just how much may be accomplished in the way of preventing acute nephritis in a given patient it is difficult to say. Yet undoubtedly the disease is often warded off by care in lessening or removing the influence of causes that are liable to produce acute inflammation of the kidney. Roughly speaking, the proper treatment of any acute infection may be regarded as prophylactic against disease of the kidney. The early and efficient use of antitoxin in diphtheria, or of quinine in malaria, will lessen the danger of nephritis. Simple sore throats deserve treatment because of the possibility of their being the starting-point of visceral complications, including nephritis. Recurrent tonsillitis may call for removal of the tonsils. A mastoiditis or a pyorrhoea may require treatment. The free use of water as a diluent

and eliminant, and attention to catharsis, may be the means of sparing the kidney undue irritation, and in this way may avoid nephritis. But knowing the remarkable tendency for this complication to appear during convalescence from acute disease, especially scarlet fever, not only should most careful attention be given the patient during the height of the disease but precautions as to diet, clothing, exercise, use of drugs, catharsis, etc., should extend well into the period of convalescence. The study of 2100 cases of scarlet fever by J. McCrae<sup>1</sup> led him to confirm the prevailing view that scarlet fever favors the development of nephritis, but at the same time impressed him with the belief that care as to diet and prolonged rest reduced the risk. Whether Mahomed is right in thinking that the onset of nephritis in scarlet fever is heralded by a rise in blood-pressure and the appearance of blood coloring matter in the urine, there should be most careful daily watching, and lessened total output, traces of albumin, or of blood, or a few casts, should be a hint for unusual care.

How far the external use of water may influence the kidneys is still a matter not definitely settled. Warm or tepid baths, sponge baths, or packs, when combined with the free drinking of water, are surely not harmful. The cold sponge or the bath in the treatment of typhoid fever is feared by some as possibly inducing congestion of the kidney. But unless nephritis already exists, the great advantages of the bath treatment of typhoid fever outweigh any hypothetical harm to the kidneys. As a matter of fact, when liquids are allowed freely, as in typhoid fever, and when the baths are properly administered, the amount of urine is increased and the amount of solids and toxins eliminated is also increased. And while the kidney is called upon to do this increased amount of work, the lessening of toxemia is one of the prime objects aimed at in the treatment of the infectious disease, and has a favorable influence in warding off nephritis. The good effect of the bath on the circulatory and nervous systems has indirectly a favorable effect on the kidney. Senator is fully convinced that bathing—even cold bathing in fevers, including scarlet fever—is not productive of renal harm.

Drugs are sometimes used so freely as remedial agents as to induce nephritis. Alcohol may be given in too large amounts. Hexamethylenamin in large doses is an irritant to the urinary tract. Special caution is necessary in the use of salicylic acid and its compounds, turpentine, copaiba, carbolic acid, corrosive sublimate, chlorate of potassium, and other remedies mentioned under the head of Etiology. Some of these may be harmful through absorption from the skin. Lüthje's<sup>2</sup> observations on albuminuria and cylindruria following the use of salicylic acid compounds are very instructive. When large doses of any of these drugs that are known to be irritants of the kidney are being given, the urine should be carefully watched, and albumin, casts or blood not interpreted in too offhand a manner as due to the infectious disease, and therefore an indication for still larger doses of the medicine

<sup>1</sup> *Trans. Assoc. Amer. Phys.*, 1913, xxviii, 194.

<sup>2</sup> *Deutsch. Arch. f. klin. Med.*, lxxiv, 163.



employed, but as possibly directly connected with the therapy. It goes without saying that prompt and proper handling of a case of poisoning by such drugs as carbolic acid, chlorate of potassium, bichloride of mercury, etc., may prevent a serious acute nephritis.

**Active Treatment.**—There is no specific for acute nephritis, no matter what its cause. The cardinal principles underlying the active treatment are: (1) The removal, when possible, of the cause. (2) Rest for the kidney, secured by throwing less work upon it, and by calling upon other organs, *e. g.*, the skin and the bowels, to do vicariously some of the work of the injured organ. (3) To treat symptoms and complications.

If the cause is remediable, as in malaria or syphilis, or when there has been alcoholic excess or too free use of irritating drugs, improvement may follow but is still uncertain; the damage to the kidney may have been serious, and even the removal of the cause may not be followed by the prompt subsidence of the renal symptoms. Yet it is the proper thing to do in every case.

The patient should be kept in bed. He should be warmly covered and may with advantage sleep between flannel blankets or wear flannel or Canton flannel nightclothes. Fresh air in the sickroom is essential, but draughts should be avoided and the temperature of the room should be about 70° F. Strict adherence to the rule of rest in bed should be enforced until the disease has disappeared. In some of the more prolonged cases, however, bed-life becomes very irksome, and some liberty in the way of sitting up or even of moving about may be permitted. This affords relief from the monotony of the recumbent posture, and while it may increase somewhat the amount of albumin in the urine, this drawback is fully compensated for by an awakening of interest on the part of the patient, an improvement in the appetite, better sleep, and better elimination.

An important question and a very live one in each individual case is that of diet. No hard and fast rule can be given applying to every case. The food should be such as will not, when its residual metabolic products are eliminated, throw too great a burden on the kidneys by reason of amount or quality. The food, too, should be such as can be easily tolerated by the irritable stomach and bowels, so often met with in nephritis, and such that its digestion is simple and not attended by the formation of faulty by-products, whose absorption may be a still further cause of damaging the diseased kidney. The food that most nearly meets the requirements is milk, and this may be given during the entire course of the disease, at first perhaps alone, later with other foods. It may be said that early in the disease it is often better to give the stomach absolute rest for a day or two, no food being allowed unless the patient craves water, of which a little may be taken. In many cases of the scarlatinal type, the onset, as already described, is more or less explosive, and among the symptoms are severe nausea and vomiting. Milk, often even water, given at such a time merely excites attacks of retching, and it is worse than useless to attempt to force the patient to take it. It is difficult to make some parents understand this point, as they feel that as the child is sick, he should at once be given medicine

to check the disease, and plenty of food to keep up the strength. But a little explanation will usually enable them to see that the starvation for a day or two is really a kindness.

The question of the *amount of water* or other fluid to be allowed an acute nephritic has been quite actively discussed, especially since von Noorden has emphasized the fact that if the inflamed kidney is to have rest, and if one of its functions in the elimination of water, the amount ingested should be restricted. The flushing-out process advocated by those who prescribe huge amounts of water he regards as unsuccessful, for the damaged organ refuses to eliminate the increased amount of water and the flushing of the tubules is not accomplished, and as illogical, because it asks an injured, inflamed part to do an increased amount of work when what it needs is a temporary rest. There is much truth in this view. The water, if given too freely when the kidneys are refusing to secrete more than four or five ounces daily, goes largely to increase the œdema. At first, then, water and milk, or other liquid as well, may with propriety be restricted to a few ounces a day. The writer has found it a fairly good rule to be guided largely by the thirst of the patient. A thirsty patient, craving water, may be given one to two quarts of fluid a day, provided the stomach tolerates it. The bowels, skin, and respiratory tract may be relied upon to take care of its elimination. The attempt to force a patient at this early stage to drink a gallon of water a day in addition to much milk is unwise. Not only will the kidney be unable to handle this large amount, but there is some danger that the flooding of the vessels may unduly strain the heart.

*Milk* as an exclusive diet cannot with advantage be continued for too long a period; it becomes monotonous, and the amount required to maintain strength is something like three or four quarts daily, an amount that few individuals will tolerate for any great length of time. To the quart or quart and a half of milk may be added, therefore, cream, which is rich in calories; and cereals may also be taken, breakfast foods, oatmeal, sago, rice, farina, etc. Fruits are not injurious, baked apples, apple sauce, orange, lemonade, grape-fruit being relished and acting perhaps as diuretics as well. A diet made up largely of fatty and carbohydrate foods leaves less residue in the shape of solids for elimination through the urine.<sup>1</sup> These foodstuffs, with but little of the proteins—possibly even less milk than is ordinarily prescribed—would seem to be peculiarly suited to cases of nephritis in which one wishes to spare the kidney excessive work. Not more than 80 or 90 grams of protein a day should be allowed, and during the acute stage less than this, say 40 or 50 grams. The amount contained in a quart of milk may be sufficient. Meat and broths should at first be forbidden. If the disease is prolonged, the craving for meat may become great and may with safety be satisfied by allowing a little meat once daily, such as a bit of bacon, chicken, fish, or even dark meat, like beefsteak, roast beef, or mutton. The prejudice against the red meats as opposed to the white has surely been largely unwarranted, and while it is unwise to allow a patient with acute

<sup>1</sup> K. N. Hansen, *Nord. Med. Ark.*, 1906, Abt. ii, No. 10.

nephritis large amounts of meats of any kind, later the taking of a small amount, even of dark meat, is permissible. Broths of various kinds and beef tea are better omitted until convalescence, as they are rich in extractives and may be injurious. Green vegetables may be taken in small quantities after the acute stage has passed, when bread and butter, toast, crackers, zwieback are allowed.

The diet, then, at first should be milk; water is allowed in moderate amounts, thirst being a fair guide as to the amount, yet a total of more than two quarts of fluid daily being rarely exceeded. Later, in addition to the milk, cereals, fruits, gruels, green vegetables, and even some meat may be added. Rich and highly seasoned or spiced foods, fried and greasy foods, the sweets, such as cakes, pastries, pies, puddings, candy, etc., are best let alone. Salt should be reduced to a minimum, especially when oedema is marked. No alcoholic drink should be allowed.

*Elimination* should be favored in every way; the kidneys should be encouraged to act, and the skin and bowels should be made the vicarious agents for performing some of the work usually performed by the kidney. Nature apparently works in this way through these channels, and also through the respiratory tract. Practically, we can imitate nature to a slight degree only in helping elimination through the respiratory tract. We may see that the patient is not deprived of his right to fresh air, which quite often, because of the overzealous efforts of attendants to prevent his "taking cold," is too rigorously shut out, and we may also by attention to the action of the heart and by not permitting pleural transudates to become too large, see that there remains no preventable hindrance to free respiratory action.

The *bowels* should be kept open. Saline laxatives are preferable when they are tolerated by the stomach. A dram to one-half ounce of Epsom or Rochelle salts or phosphate of soda, taken in half a glass to one glass of water the first thing in the morning, will usually secure free watery movements of the bowels, and may also lower blood-pressure. Many of the natural or prepared saline laxative waters will answer equally well, *e. g.*, Hunyadi, Rubinat, Carlsbad, etc. In other instances the vegetable laxatives taken at bedtime seem to work better, *e. g.*, cascara, senna, or the pill of aloin, strychnine and belladonna. An occasional calomel purge is often very beneficial, and, especially when nausea is extreme, the use of calomel in often-repeated small doses (gr.  $\frac{1}{10}$  to gr.  $\frac{1}{2}$ , gm. 0.006 to 0.03) will move the bowels and at the same time act helpfully in allaying the nausea. Brisker and more promptly acting cathartics may be required, especially when acute uremia seems impending, and under these circumstances elaterium or elaterin (gr.  $\frac{1}{20}$  to gr.  $\frac{1}{10}$ , gm. 0.003 to 0.006), compound jalap powder, or even a drop or two of croton oil may be used. Elaterium too long continued irritates the stomach, and may be depressing. Enemas may prove of material help in keeping the bowels open, but in general in acute nephritis a little more thorough cleaning out of the alimentary tract is desired than that brought about by enemata.

All *diuretics* are liable to fail in acute nephritis, as the kidneys are in such condition that they will not respond to any influences. Milk



and water are among the simplest and best diuretics. Lemonade is also excellent, and to this may be added cream of tartar, one teaspoonful to the pint of lemonade, the cream of tartar being first dissolved in hot water, as it is poorly soluble in the cold. The lemonade thus prepared is taken cold or hot, as the patient prefers. If taken freely, this is diuretic and laxative. With a weak heart and low blood-pressure, digitalis and caffeine are of service in increasing the flow of urine. The citrate or acetate of potassium or sodium may be given in doses of from 10 to 30 grains (gm. 0.6 to 2) to an adult, and seem to be non-irritating. Excreted as carbonates, they tend to alkalinize the urine and also increase its flow. Sodium theobromine salicylate (diuretin), in doses of 60 to 90 grains (gm. 4 to 6) a day, is sometimes efficient, although its effects are often limited in acute nephritis, where the renal epithelium has undergone so great damage. Diuretin, like caffeine, is of special value when the heart is weak. Theocin, gr. iij (0.2 gm.) in a capsule, is also valuable. Cantharides, copaiba, cubebs, turpentine, that are sometimes advocated as diuretics, are far too irritating to the kidneys to be employed. Even gin, the household diuretic, is best avoided. And it is well not to push to the limit some of the simpler diuretics, such as the citrates and acetates, because of a possible harmful influence. Experimental work along this line, while inconclusive, suggests caution in the use of diuretics in nephritis.<sup>1</sup> The writer has seen good diuretic results, with lessening of toxic symptoms, follow the use of Fischer's solution in acute nephritis.

Due attention should be paid to the *skin*. Not only, as has already been stated, should it be kept warm, draughts and exposure to cold being avoided, but efforts should be made to secure free diaphoresis as a means of elimination. The amount of toxic material got rid of in this way may not be great, but there is some that escapes with the sweat. Patients, as a rule, express themselves as feeling better, and they have that appearance, and blood-pressure may be lowered. Simple lukewarm or hot tub baths, or, if the patient is too weak, sponge baths, are of benefit. A sitz bath or a good soak in a tub of hot water, followed by a rubdown and immediate rest in a warm bed, is often the means of promoting free action of the skin and also of the kidneys. If quite hot water be employed, it is well to keep a cool cloth to the head during the bath. If thirsty, the patient may take a drink of water or of lemonade. The hot bath or the sweat bath in nephritis must be watched. Occasionally a patient does badly, becomes cyanotic, feels faint, and has a feeble pulse. Such patients must be given a shorter bath or a lukewarm one only, or this plan of treatment must be given up entirely.

*Sweats* are especially indicated when œdema is marked. Any procedure may be legitimately employed that will induce free action of the skin without inducing too great weakness and without exposing the patient to the subsequent influence of cold. The objection to pilocarpine (gr.  $\frac{1}{10}$  to gr.  $\frac{1}{6}$ , 0.006 to 0.01 gm.) is that it is a cardiac depressant. It will induce profuse diaphoresis. But an effect not desired is a profuse bronchial secretion; with the weakened heart too many of the phenomena of

<sup>1</sup> Mosenthal and Schlayer, *Deutsch. Arch. f. klin. Med.*, 1913, Bd. iii, p. 217.

œdema of the lungs become manifest, either for the good of the patient or the mental comfort of the physician. Occasionally in patients who sweat poorly by the external application of heat a small dose of pilocarpine (gr.  $\frac{1}{12}$ ) may be given hypodermically as an adjuvant. Large doses are certainly dangerous. It is to be remembered that pilocarpine once given differs from the ordinary means of inducing sweating, for its effects cannot be checked at will. With sweating by external means the further continuance of the diaphoretic measure can be promptly stopped if untoward effects are noticed.

Various means for applying *heat* externally have been devised. A simple measure is to have the patient sit on a cane-seated chair, with a blanket pinned about his neck, thus making a tent covering the body below that point, and then to place a lighted alcohol or kerosene lamp beneath the chair. After a short time the body drips with sweat. Care must be exercised not to blister the patient and not to set fire to the blanket or clothing. Electric-light baths are an efficient means of securing the result. When patients are too weak to sit up, some means for sweating them in bed must be employed.

A method easy of application is to make a tent of blankets, canvas, or rubber sheeting over the patient, the blankets being held up by supports, such as half barrel-hoops. Into this tent a stovepipe of narrow caliber, such as any tinsmith can furnish, is conducted. This pipe, by an elbow, reaches nearly to the floor, and under its lower opening an alcohol or other light is placed. By this means the heated air is conducted into the tent in which the patient is lying, and a sweat is easily given. The method in vogue in the Presbyterian Hospital in Chicago serves admirably. The patient lies between blankets, and outside each blanket, the one under as well as the one above the patient, is a heavy rubber sheet. Hot bricks, in bags for convenience of handling, are placed about the patient, the blanket being so rolled that the body is protected from the brick by the cloth of the bag and by the thickness of the blanket. Alcohol is poured over the bricks and the blankets tucked in around the patient. A cold cloth is kept on the forehead during the sweat. A drink of lemonade is given before the sweat and during it, if the patient desires. In from twenty minutes to an hour, the length of time depending on the amount of sweat, the condition of the pulse, and the comfort of the patient, the procedure is stopped, the bricks are removed, the patient rubbed dry, and the damp blankets being taken away he is left on the warm dry sheet that has been previously arranged beneath the lower rubber blanket. Sweats of one kind or another may be given once or twice daily, or less often, depending on the degree of œdema and the effect on the patient. If the patient is comatose unusual care must be exercised not to blister or burn.

*Complications* and annoying symptoms must be treated as they arise. Some of these, including uremia, will be discussed more fully in treating of chronic nephritis. The œdema may demand not only the sweats but puncture of the legs, paracentesis of the abdomen or of the pleura. Edema of the larynx occasionally necessitates scarification or even tracheotomy.

Drugs supposed to act as specifics in acute nephritis are of no benefit whatever, and it is useless or even harmful to give large doses of tannin, ergot, or methylene blue in the hope of effecting a cure. Surgery (acupuncture, splitting the kidney, decapsulation, etc.) has a very limited field in the treatment. This will be taken up later.

*Pain* over the kidney is often relieved by the hot-water bag, the electric pad (heat), or by mustard paste. Blistering is unnecessary. At times vigorous counterirritation seems to relieve not only the lumbar pain but an increased flow of urine is excited; the congestion of the kidney seems to be somewhat lessened. Severe headache occasionally requires bromide or even morphine. The latter drug should in general be used sparingly in acute nephritis, but in some instances the effect is to increase the output of urine rather than to diminish it.

After the acute stage much good may come from the use of some of the bitter tonics. Appetite and digestion may be much improved by nux vomica and hydrochloric acid. When anemia is marked, and especially when convalescence is delayed, iron is of great value. Some of the scale preparations of iron may be employed, or Bland's mass, or even the tincture of the chloride of iron, although this preparation is not always well tolerated by the stomach. It is here that Basham's mixture (*mistura ferri et ammonii acetatis*) may serve a useful purpose. It is not unpleasant to take, is non-irritating, and in doses of  $\overline{5}j$  to  $\overline{5}iv$  (4 to 15 cc.) often acts not only as a hematinic but as a diuretic.

Cardiac stimulation may be necessary. Strychnine is here of service, and digitalis especially when blood-pressure begins to fail. This remedy as well as strophanthus and caffeine have also the effect of increasing the flow of urine.

Practically nothing has been accomplished in the way of treating acute nephritis by specific bacterial products. Yet if microbic etiological factors can be definitely identified as the cause of a given case of nephritis there may be promise in the use of specific sera or of the so-called vaccines. Some measure of success will, it is to be hoped, attend the attempt in such cases to remove the operating microbic cause. Microbic pyelitis may be treated with specific serum or vaccine—and work of this kind has been done in this condition—and consecutive nephritis be prevented or ameliorated. The possible damaging effects of specific sera and vaccines on the kidney are matters for careful consideration.



## CHAPTER XVI

### CHRONIC NEPHRITIS AND AMYLOID DISEASE OF KIDNEY

BY JAMES B. HERRICK, M.D.

#### CHRONIC PARENCHYMATOUS NEPHRITIS

THE term parenchymatous is in a sense a misnomer, as the pathological process is *always diffuse*, and the type, as already stated, shades imperceptibly on the one hand into the acute form, and on the other into chronic nephritis with induration and contraction. The description of this form may be made rather brief, as in many respects that already given of acute nephritis will apply to the chronic parenchymatous form.

**Etiology.**—In most cases no definite cause can be assigned. Some factors, however, that when operating suddenly or with great intensity produce acute nephritis, may, if operating for a longer period or less severely, produce the chronic form of the disease. Long-continued exposure to *cold* explains its not infrequent occurrence in those who live or work in damp cellars, also its occurrence in bakers, butchers, and icemen. *Alcoholism* may also produce it. The acute *infectious diseases*, such as scarlet fever and malaria, which oftener produce the acute form, are said by many to produce the chronic form at times, or the acute form passes over into the chronic type. Malaria has been regarded by many—Rosenstein, Bartels, Thayer, and others—as a frequent cause of this type of nephritis. On the other hand, Wagner and some other writers dispute this fact. While direct proof that the *gonococcus* is the cause of acute or chronic parenchymatous nephritis is not easily available, the writer believes that it may occasionally produce such an inflammation. Lurking in the prostate, the joints, or the Fallopian tubes, it may by systemic invasion and long after the acute manifestations have disappeared give rise to acute or chronic inflammatory inflammation in various organs or tissues, and among these may perhaps be, oftener than we think, the kidney. *Chronic intoxications*, where one must assume the condition of altered blood, may produce irritation and ultimately inflammation of the kidneys. It is seen occasionally in lead or mercurial poisoning; also in connection with syphilis, diabetes, or suppurating disease.

Making allowance for the cases of acute nephritis and of amyloid disease that have been wrongly classed as chronic parenchymatous nephritis, the fact remains that *pulmonary tuberculosis* is one of the most frequent causes of chronic parenchymatous nephritis. Occasionally, in connection with valvular heart disease, the condition of *cyanotic induration* or chronic passive congestion seems to give rise to this form of Bright's

disease, although, as Rosenstein and Senator have suggested, there is a possibility that the heart disease and the kidney disease are due to one and the same cause, rather than that the lesion in the kidney is entirely secondary to the cardiac condition.

**Pathological Anatomy.**—As already stated, the process is always diffuse and never limited solely to the parenchyma proper. It is largely owing to these varying degrees to which the interstitial fibroid process is present that several varieties of chronic parenchymatous nephritis have been described. What may, perhaps, be regarded as the type is the *large white kidney* of Wilks. This kidney is enlarged, weighing about 250 to 300 grams (Fagge mentions a pair of kidneys weighing 29 ounces), light gray—even almost white—in color, the stellate veins showing distinctly. The kidney is soft, and on section the thin capsule is found to strip readily, leaving a non-granular surface. The cortex is swollen and pale yellow or grayish. The dark pyramids with their streaked markings show in striking contrast to the light and more homogenous-appearing cortex. The cortical markings are usually indistinct, and dull opaque spots or streaks are often to be made out in the midst of the more translucent areas. Minute reddish dots may be occasionally seen, due to hemorrhages (chronic hemorrhagic nephritis).

*Microscopically*, there is a marked degenerative change in the *epithelium* lining the tubes, especially marked in the convoluted tubules. Individual cells are swollen, granular, fatty, with outlines often indistinct. The nuclei may be fragmented or invisible. The swollen cells may narrow the lumen of the tube, or by their desquamation the caliber may be increased. Casts of different kinds, epithelial cells in various stages of degeneration, granular debris, fat globules, and red and white blood corpuscles, may crowd the tubule.

The *Malpighian bodies* show varying changes, much as in acute nephritis. They are usually enlarged. Epithelium with fatty degeneration is often seen in the glomerulus proper and in the capsule. Proliferative change with nuclear multiplication is frequently one of the striking lesions. Swollen, desquamated and degenerate cells may fill the capsular space, and the capsule may be denuded or exhibit a lining of freshly proliferated cells. Red and white corpuscles may crowd the space (hemorrhagic form), or it may be distended with a clear inflammatory exudate, pushing the capillary tuft to one side. The wall of the capsule may be thickened, and in some instances show slight fibrous growth. The capillaries may show hyaline changes in their walls and are often thrombosed.

The intertubular *connective tissue* shows varying degrees of oedema. Round-cell infiltration may be here and there present. Small hemorrhages may have occurred; in these cases pigment granules may be seen in the connective tissue (Ziegler).

Many variations from this type of the large white kidney have been described, being dependent partly on the color, consistency and size, and partly on the degree of fibroid change present. The predominance of fatty changes produces the white or grayish color. If this kidney at the same time has somewhat advanced interstitial changes with

contraction, it is smaller, firmer, the capsule thickened and adherent in places, and the surface rough and granular. Bowman's capsule will show thickening and the glomerulus itself may be atrophied or its place taken by fibrous tissue. This is the *small white kidney*, a combination apparently of the fatty degenerative process with marked induration as well, the latter at times a sequel of the earlier parenchymatous change—*secondary contracted kidney*—though in some instances these processes are perhaps coincident. Some of these kidneys are above the normal in size, and are, therefore, in the strict sense not contracted.

In all these forms the kidneys are not uniformly affected, markedly involved areas often appearing in the midst of seemingly healthy tissue. Some describe as a separate variety of chronic parenchymatous nephritis a kidney of large size, mottled with reddish and light areas—representing respectively small hemorrhages or highly vascular areas, and fattily degenerated and relatively anemic tissue—with slightly adherent capsule, the organ being firm from abundance of connective tissue. This is the large red kidney, or *variegated kidney*.

**Symptoms.**—The striking features in the clinical manifestations of chronic parenchymatous nephritis are the slow, insidious onset, the characteristic urinary findings, and the marked degree of œdema. In most instances the physician is consulted either because of vague, indefinite symptoms, such as malaise, poor appetite, disturbance of the stomach or bowel, general weakness, or because some puffiness has been noted about the eyes or about the ankles.

**The Urine.**—The amount is diminished. On an average, perhaps 500 cc. would be the daily output. The specific gravity in general is normal or slightly above normal. The urine is acid, dark, often turbid. Occasionally there is a distinct opalescence from the presence of numerous fat globules. On standing there is an abundant sediment which consists largely of urates, casts, white- and red-blood corpuscles, epithelial cells, and amorphous debris. The reaction for albumin is prompt and shows a large amount. This is particularly true of the day urine. The quantity is ordinarily from 0.5 to 2 per cent. The total amount lost during the day will run anywhere from 5 to 30 grams. Exceptionally, larger amounts than this have been noted. The urea and solids are diminished absolutely. Relatively, however, they are usually in normal or even increased amount. In case improvement occurs, or there is the development of the secondary contracted kidney, the amount of urine will increase sometimes to as much as 5 or 6 liters. The specific gravity will be greatly lowered and the percentage of albumin will be decidedly lessened. The absolute amount of solids will be increased. The freezing-point of the urine in this form of nephritis is sometimes lower than normal, although it is influenced much by the degree of œdema and anemia, the blood-pressure, etc. Rarely it will be found as low as  $-2.6^{\circ}\text{C}.$ , oftener in the neighborhood of  $-1^{\circ}\text{C}.$  As an aid in the diagnosis of chronic parenchymatous nephritis cryoscopy is of little value.

The microscopic study of the urine shows casts of nearly every variety. Hyaline and granular casts are abundant, and many of the latter are dark in color and contain coarse granules. Numerous broad casts are



also seen. Waxy casts and casts with oil globules upon them are very common. Renal epithelial cells, many of them showing marked degenerative changes and covered with fat globules, are found in abundance. Occasionally cases are reported in which casts are said to be absent, even though the amount of albumin is abundant. This may exceptionally be true, but the explanation is perhaps to be found in faulty technique, or in the fact that the urine is old or has undergone decomposition in the bladder. That casts may be dissolved by the presence in the urine of some pepsin-like body has been shown by Sehrwald.

**Œdema.**—The œdema in this form of Bright's disease usually begins rather slowly and is first noticed as puffiness of the eyelids in the morning or about the ankles at night. It gradually increases, however, until we find the patient in the marked cases presenting an extreme degree of anasarca, with the face swollen, and wrinkles that give expression to the countenance obliterated, the hands, the arms, the back, the legs, all showing marked œdema. One of the most annoying and one of the most striking complications is the œdema of the loose tissue of the penis and scrotum. This may be extreme and even cause some difficulty in urinating. The serous cavities often contain fluid. Rarely there is a localized œdema, and one sees the collection of fluid limited to one pleural cavity, to the scrotum, or to the legs. Together with the œdema there is more or less anemia. This is due to the fact that the red-blood corpuscles and hemoglobin are actually diminished, and also to the fact that the blood is thinned because of the condition of hydremia. The capillaries also are spread out over a more extensive surface, so that the anemia is apparently greater than it really is. With the œdema the anemia gives to the patient a peculiar puffy, pasty-like appearance which is quite characteristic, and enables one sometimes to make a diagnosis almost at a glance. The œdema, when extreme, causes a marked increase in the weight of the patient. When it disappears, the patient is seen to be greatly emaciated, and the skin hangs in loose folds where before it had been tense with the accumulated fluid.

The waterlogged condition of the wall of the stomach and of the bowel interferes seriously with the performance of function of these two organs. The pressure of the fluid in the pleura and pericardium, as well as the upward pressure of the fluid on the diaphragm, when ascites is marked, interferes very much with the action of the heart and of the lungs. The patients are frequently obliged to sit up at night in order to breathe. The swollen condition of the legs and thighs, together with the general weakness, make it impossible for some of them to move about with any degree of comfort, so that their life really consists of lying in bed or sitting up in a chair. The tense skin may rupture or become abraded, and then, if infection occurs, serious inflammation may result.

Reference has been made to the gastro-intestinal disturbance that comes from œdema. While œdema does not explain all of the disturbance, there is no nephritis in which the digestion is more interfered with than in this form. The appetite is often poor, and patients have a loathing for ordinary simple food. There is nausea, not infrequently vomiting; a feeling of fulness and weight amounting to positive distress

or pain is sometimes complained of after eating. The bowels may be constipated, but are often loose; ulceration of the intestine is occasionally an explanation for this diarrhœa. The tongue is coated; there is a fetid odor to the breath. This poor digestion is one reason for the great loss of strength, for the anemia and for the emaciation.

Changes in the *heart* and *bloodvessels* are commonly present, although they are by no means so marked as in the cases of chronic interstitial nephritis. They may be entirely absent. If secondary contraction occurs, then cardiovascular changes may become pronounced. The dyspnœa of which these patients complain is often cardiac in origin from dilatation or myocardial degeneration, although the anemia, œdema, and uremia as well may contribute to produce the shortness of breath.

*Uremia* is generally present, and while not such a striking feature as in some cases of acute nephritis, or in the typical chronic interstitial nephritis, still offers the explanation of many of the symptoms complained of by these patients. The malaise, some of the gastro-intestinal disturbances, headache, sleeplessness, are in many instances undoubtedly uremic in character, and as the disease goes on some patients have definite uremic manifestations in the shape of almost unbearable headache, convulsions, or coma. Retinitis and optic neuritis may occasionally be seen. Rarely the amaurosis not infrequently met with in the contracted kidney is seen in this form of Bright's disease.

In some cases, after the evidences of chronic parenchymatous nephritis have lasted for many months, a change occurs which is quite remarkable, the dropsy becoming less, and finally entirely disappearing, the urine increasing in amount, becoming lighter in color, lower in specific gravity, and containing a smaller number of casts and a smaller percentage of albumin. The condition of *secondary contracted kidney* has now appeared, and while the patient may flatter himself that he is decidedly better, or even entirely well, the careful physician will find on examination that the urine is still albuminous and contains a few casts. Hypertrophy of the left ventricle with increase in blood-pressure will also be present though in some instances the cardiovascular changes may be lacking. The manifestations of uremia appear, and the case runs the course of an ordinary contracted kidney. Through this somewhat favorable termination of chronic parenchymatous nephritis life may be prolonged for many months, sometimes for several years.

**Complications.**—The complications referred to under the head of acute nephritis are practically those that are met with in chronic parenchymatous nephritis. Pneumonia, bronchitis, or œdema of the lungs may become serious and even the cause of death. Inflammation of the serous membranes—pleuritis, pericarditis, peritonitis—is met with. Intercurrent infectious, like erysipelas, may occur. Death is brought about at times from dilatation of the heart or from myocardial weakness. Alimentary disturbances in the shape of acute gastritis or enterocolitis may be serious complications.

**Diagnosis.**—There is no difficulty whatever in diagnosing the existence of nephritis in cases of the type under discussion, provided the urine is

examined. An abundance of albumin and casts leaves no question as to the existence of nephritis. The marked œdema also helps in making this diagnosis. The only question is as to the variety.

From *acute nephritis* the differentiation is often impossible unless one knows the early history. An abundance of red-blood corpuscles in the urine speaks for acute nephritis. Yet it must be remembered that in the chronic form microscopic blood may be found and occasionally a hemorrhagic type is seen with frequent renal hemorrhages causing hematuria of such severity as to be noted by the naked eye. In many cases, however, an attempt to differentiate between the two is unavailing, and one must be satisfied with saying that one is dealing with parenchymatous nephritis without trying to tell whether it is acute, subacute, or chronic.

From *chronic interstitial nephritis* of the typical variety the differentiation is easy. The abundance of albumin and casts, the marked œdema, the slight degree of cardiovascular changes, are all in such striking contrast to the marked cardiovascular changes, the absence of œdema, the large amount of urine of low specific gravity and small amount of albumin and casts that are met with in contracted kidney, that the differentiation is simple. When *secondary contracted* kidney exists, differentiation from the primary contracted kidney is made by the preceding history of œdema and marked albuminuria. Yet many of our efforts to fit these cases of nephritis into definite pigeon-holes and label them as chronic parenchymatous or chronic interstitial nephritis are really useless because, as has been said, the cases often from the beginning are of a more diffuse character and present the characteristics of both types of disease. The best diagnosis that can be made here is chronic nephritis or simply *chronic diffuse nephritis*. Many cases from the onset show some cardiovascular change and have uremic symptoms, perhaps retinitis, like the chronic interstitial variety; but they show the œdema of renal origin, a urine rich in albumin and casts, and often of a specific gravity that is about normal or perhaps just a little below normal. To a case of this kind the name *chronic nephritis*, without any qualifying adjective, had best be applied, or one may employ Müller's expression and speak merely of a chronic disease of the kidney with dropsy.

From *amyloid* kidney the differentiation is not always easy, and is sometimes impossible because the two diseases may be combined. Amyloid may be suspected, however, when any cause for amyloid, such as syphilis, tuberculosis, or chronic suppuration, exists, and when, along with the urinary findings, an enlargement of the spleen and liver can be made out. In amyloid, too, cachexia is more pronounced and there is generally less universal dropsy. The urine may show variations in amount, and casts are apt to be fewer than in the chronic nephritis. Serum globulin is present in increased proportion. Uremia and retinitis are relatively rare.

From *congestion of the kidney* the differentiation is usually easy, the œdema being in the lower part of the body, and there being a definite cause for the congestion, such as a weak heart. The amount of albumin is usually less than in the true nephritis; the casts are fewer, and the



therapeutic test—rest and cardiac stimulants, with resulting improvement in the urine—will usually clear up the diagnosis.

**Prognosis.**—This form of disease was once looked upon as entirely hopeless. Even now the prognosis is justly regarded as extremely bad. The collective report of Cabot, made a few years ago, showed that many physicians of good repute had seen stray cases of recovery from chronic parenchymatous nephritis. The question always arises in these instances as to where to draw the line between acute nephritis, which admittedly often gets well, and the genuine chronic parenchymatous form of the disease. Dropsy has been looked upon as having an important bearing on prognosis, but there seems to be no rule as to this, and the case that is accompanied by severe dropsy may have as good a prognosis as the one in which it is not so very marked. Some of the supposed recoveries, if carefully looked into, will be found to be instances in which the secondary contracted kidney has developed. In chronic parenchymatous nephritis spontaneous improvement and relapse are not uncommon events. Death occurs from exhaustion in the greatest number of cases, this being brought about by inability to take, digest, and assimilate food, by the anemia, and by the consequences of œdema. Death may also be brought about directly through the weakness of the heart, through some uremic manifestations, such as convulsions or coma, or through some of the numerous complications already mentioned. Few patients live longer than two years.

**Treatment.**—In the way of *prophylaxis* little can be done in any individual case, although the chronic alcoholic may be cautioned against the possible effects of his bad habits, and the worker in cold, damp places may be advised of the dangers of exposure to extremes of heat and cold; but in practice very little can be done in the way of prophylaxis.

In general, the *active* treatment is the same as in the acute form of the disease. *Rest* is of great importance. Rest in bed is usually instituted at the beginning of treatment, and the result commonly is that the albumin diminishes and the patient is better for the time being. Rest here should not be too absolute, however, and not be continued for too long a time. It becomes extremely irksome and monotonous, and when the disease is going to last for many months, one cannot expect a patient to stay in bed during all this period. It is much better, at times, to let the patient sit up and even indulge in a little exercise about the house, or in pleasant weather go outdoors; there is often a distinct gain in the appetite and digestive power; the patient sleeps better and the anemia is improved. The patient should be warmly clad and avoid exposure to cold. Woollen garments should be worn next to the skin.

The question of *diet* is an important one, and what has been said regarding acute nephritis will apply to chronic nephritis, yet the same restrictions cannot be enjoined for so long a period. We cannot, in other words, keep the patient for months upon an exclusively milk diet. If we do, we find that the appetite disappears; nausea and diarrhœa are apt to occur, and there is great loss of strength and deterioration of the blood. Milk can, however, be one of the main articles of diet, and a patient may take with profit say a quart of milk daily, but in addition

there should be other foods. Meat may be allowed in small amounts, perhaps once a day. The daily total protein intake should not be less than 80 grams nor much in excess of 100 grams. In this way the needs of the body are met without drawing upon the body proteins and there is no tax upon the kidney because of excessive amount of protein ingested. One quart of milk contains about 60 grams of protein. It makes little difference whether the meat be light or dark. Cereals, such as oatmeal and the ordinary breakfast foods, rice, sago, farina, tapioca, may be allowed freely. Fruits are also in order. Lemonade is a good diuretic and is frequently enjoyed by these patients. Some of the simpler vegetables may be taken. Broths should not be rich nor contain too much meat juice. Gruels made up with water or with milk are not harmful. Fried and greasy foods; sweets, such as cakes, pastries, pies, candies, and desserts; all rich and highly seasoned foods, should be omitted or taken in very small amounts. There is seldom any danger of the patient's overeating because the appetite is usually so poor that the endeavor is rather to get the patient to eat enough than to prevent him from taking too much.

*Water* should not be taken in excessive amounts; it is not eliminated freely through the kidney, and tends to increase the œdema. Whether or not water be regarded, in part at least, as a metabolic product, the fact is that the diseased kidney has lost its power of passing large amounts of water rapidly from the body, it has lost its "diluting power" (Koranyi), or elimination is, at least, delayed (bradyuria), so that an increase in the intake of water results not in polyuria but in an increase of œdema. When, however, œdema is disappearing and polyuria has set in, one may assume more nearly patent glomerular vessels and tubules and a restoration of renal function in the way of power of eliminating water, and the amount of water ingested may now be increased and will be followed by a corresponding increase in the amount of urine. The rule is a fairly good one to let the patient take such water, milk, and other fluids as his thirst indicates. One and one-half to two quarts of fluid a day will represent a fair allowance. Wine, beer, and the stronger alcoholic drinks should not be allowed unless it be in exceptional cases, where a little wine may be allowed with meals. Smoking is not necessarily to be prohibited. The morning cup of coffee is something that patients usually cling to, and, as a rule, there is no harm in allowing this.

*Sodium chloride* is frequently eliminated poorly by the inflamed kidney. Whether sodium chloride retention is a potent cause of œdema, the chloride being held in the body tissues, or whether both are merely phenomena of nephritis, with no relation of cause and effect, is a subject needing further investigation. Yet so many suggestive facts have been noted, the rapid fall of sodium chloride in the urine when ascites suddenly develops, its increase in the urine when œdema is disappearing, the production at will of a rise and fall of the œdema by increasing or lessening the amount fed—and retained—to patients who have been experimentally observed, that one feels that there are many things that go to show a disturbance of water balance and alterations in osmotic pressure from chloride retention, that might easily result in an increase of

fluid in the intercellular tissues. The amount of salt necessary in the body is usually supplied by that found in the bread and milk ordinarily ingested. While one cannot make any extravagant claims for the treatment of the œdema of nephritis by the withdrawal of salt—dechlorination—still the investigations of Widal, Javal, Strauss, and many others seem to indicate that in some cases, at least, an ordinary or excessive amount of salt in the food increases the œdema and albuminuria, while a reduction of the amount tends to lessen the same. It is wise, therefore, to limit the amount of salt ingested.

A point that is often not insisted on enough is that a patient with nephritis should be allowed the benefits that come not only from good food, but from fresh air. The fear of taking cold very often leads the patient to shut himself indoors and to deny himself the privilege of fresh air. A change of *climate* will sometimes benefit these patients. Going to a warm, dry climate, the patient can be in the open air, and in that way he is greatly helped, as elimination through the skin by invisible sweating is much greater.

The *anemia* of this form of nephritis is combated not only by the fresh air and the food but usually by the giving of iron. Some contend that very large doses of iron should be given—30 to 60 drops of the tincture of chloride of iron—after meals. Iron is of great benefit in these cases, but the writer believes that James Tyson is right when he says that “large doses of iron should not be given. They are useless; lock up the secretions, cause headache, and increase the danger of uremia.” The writer gives *Basham's mixture* oftener than any other preparation of iron. This is easily tolerated by the stomach, is not at all unpleasant to take, and seems to have some diuretic action as well as to act favorably in improving the anemia.

Elimination in this form of nephritis is secured, as in other conditions, largely by the use of *laxatives*. Almost any laxative may be given, but the salines seem to act the best. The saline cathartics may be given on an empty stomach early in the morning, and enough should be taken to induce two or three rather loose watery stools. At times good follows from giving the saline several times during the day, or from using some of the stronger cathartics, like elaterin. This vigorous purging is apt to be rather depressing, and it is not always wise to secure a reduction in the œdema at the expense of the strength of the patient. Some of the vegetable laxatives, like cascara or senna, are of value, or phenolphthalein may be used at night (gr. ij to v, 0.12 to 0.3 gm.) or smaller doses three times a day.

The reduction of the œdema by means of *sweats* has already been referred to under the head of Acute Nephritis. It is of interest to note that Bendix<sup>1</sup> finds in cases with the molecular concentration of the blood increased and the freezing-point lowered that there is a tendency toward lessening of molecular concentration and an approach toward normal of the freezing-point by the use of sweats. When this is normal, however, no change is brought about by sweating. Fear has been

<sup>1</sup> *Deutsch. med. Woch.*, 1904, No. 7.



expressed by some lest by sweating a too great concentration of toxins in the blood might result. Leube, for one, advises that liberal amounts of water be taken at the time a sweat is given, so that this tendency may be counteracted. Sweats may be given in any way that is most feasible. Many patients will get into the tub and take a hot bath at a temperature of 103° to 105° F., and then roll up in warm blankets in bed and sweat profusely. This is a very simple method. The sweat may be induced by the hot pack. The bath by means of the hot bricks, as described under the head of Acute Nephritis, is a simple method and especially suitable for hospital use. The electric light bath, or even the Turkish bath, where there are proper establishments, and where care can be given to the patient afterward to insure a prolonged period of rest and to see that he does not go out into the open air too soon, are methods of inducing sweat that are very efficient. Some patients undoubtedly derive great benefit from the sweat given once or even twice a day. The physician must judge in each case as to how long the sweat should continue as well as how often it should be given.

Œdema very often calls for *aspiration* of the pleural or abdominal cavity, or puncture of the skin. When there is double hydrothorax of any considerable extent, and when dyspnœa is pronounced, aspiration should not be long delayed. With double hydrothorax sudden death has been met with more than once. While the fluid may reappear, still the drawing off of one quart or one quart and a half from the pleural cavity relieves the pressure upon the lungs, vessels, and the heart, and absorption is sometimes quite rapid after the aspiration. So, too, tapping of the abdomen is oftentimes followed by great relief in every way.

The question of *draining the legs*, when the œdema is extreme, is one that arises very often, and the physician hesitates to make a puncture through the skin of the leg, knowing that the wound will remain open for many days and that there is great danger of infection. When a patient can have the services of a trained nurse, and when asepsis can be rigidly carried out, these punctures may be made with much more freedom than under other circumstances. The good results are sometimes very striking. Fluid oozes for many days, and the œdema of the lower extremities disappears as well as the œdema of the scrotum, and to a certain extent the ascites and œdema of the abdominal wall. The operation may be done in one of three ways. The writer prefers many small punctures through the skin, made with the ordinary scalpel. Some prefer to make one large cut two or three inches in length down to the bone over the skin, while others prefer the use of the Southey tubes. Anyone of these methods is successful, and the dangers from one are about as great as from the other.

Attention should be paid to the condition of the *heart*, and the use of strychnine, digitalis, or strophanthus is sometimes clearly indicated. The good effects of digitalis are often seen in the increased elimination of urine as well as in the improvement in dyspnœa. Sleep is frequently disturbed in nephritis and may necessitate the use of bromides, or some of the *hypnotics*, like veronal or sulphonal. Morphine, or some other derivative of opium, in small doses is occasionally the best hypnotic

to give. One must be very careful in using this not to give too large doses, and should also be careful not to induce the morphine habit. But there are many patients for whom a hypodermic of morphine given at night is the very best hypnotic to employ. Pain is rarely so great as to demand opiates. Sometimes the headache is extremely severe, and here opium will be called for. The treatment of the uremic complications, such as coma and convulsions, is the usual treatment referred to elsewhere.

### CHRONIC INTERSTITIAL NEPHRITIS.

**Introduction.**—As already stated, three divisions of this form may be made: (1) Primary chronic interstitial nephritis; (2) secondary chronic interstitial nephritis; (3) arteriosclerotic kidney.

It is no easy thing to classify these cases as they come to the physician, or even as the kidneys are studied in the dead-house. Secondary contracted kidney may closely resemble the primary form, and only a knowledge of the previous clinical history may enable one to recognize the true character. The relation of the renal lesion to the arteriosclerosis found during life and postmortem may be difficult to unravel. Three explanations are possible: (1) General arteriosclerosis may be primary, the kidney being secondarily involved. (2) The arteriosclerosis may be a result of primary renal disease that leads to cardiac hypertrophy and high blood-pressure, *i. e.*, there is primary nephritis with secondary arteriosclerosis. (3) Or the vascular and renal conditions may be due to one and the same cause, developing independently of each other yet simultaneously. It may be added that some—and with much reason—object to the use of the term nephritis, implying as it does an inflammatory process, for in many of these kidneys there is more of atrophy with secondary fibrosis than of true inflammation. Such terms as granular kidney, contracted kidney, sclerotic kidney, cirrhotic kidney, are employed to describe this form or some modification of the same.

**Etiology.**—The causes of chronic interstitial nephritis of the secondary type are those already enumerated for the chronic parenchymatous form. The arteriosclerotic kidney has its etiological factor in any of the conditions that lead to general arteriosclerosis—lead, gout, syphilis, alcohol, heredity, severe muscular strain, overwork, worry, etc.

Several years ago Rosenstein wrote that for the overwhelming majority of cases of genuine contracted kidney we know no cause. This statement holds to-day. Yet some facts seem fairly well established. The origin is in many, probably most, cases hemic, through the presence in the blood of material that acts on the kidney as a toxic irritant. Some of the causes enumerated for acute nephritis might, if long continued in milder degree, produce the chronic inflammation. Some French writers (Brault) recognize this by speaking of chronic interstitial nephritis as *nephrite par intoxications lentes*. Exceptionally an acute nephritis is the starting-point; a scarlatinal nephritis, for example, passes gradually into the contracted kidney. Dickinson<sup>1</sup> described such cases.

<sup>1</sup> *Allbutt's System*, 1897, v, 376.

*Heredity.*—A hereditary tendency to chronic nephritis is undoubtedly seen at times. Reference has been made to an example of this in a woman with contracted kidney whose three daughters and one son show albumin and beginning nephritis, and several of whose ancestors had chronic nephritis. Dickinson, Eichhorst,<sup>1</sup> Kidd<sup>2</sup> A. V. Meigs,<sup>3</sup> Pel,<sup>4</sup> and Frölich<sup>5</sup> report family and hereditary nephritis. Tendency to early arterial degeneration is often hereditarily transmitted. In some families this is seen in cerebral hemorrhages; in others as myocarditis or pectoral angina, or again as contracted kidney. Or one member of the family exhibits one manifestation of the disease, *e. g.*, the myocardial, while another has cerebral hemorrhage, and another has chronic nephritis. Not infrequently in one and the same individual there may be manifested not alone the nephritis, but the myocardial or cerebral evidences of arteriosclerosis.

*Congenital contracted kidney* has been reported by Weigert and by Hellendahl. In childhood chronic interstitial nephritis is relatively rare, yet it has been seen by many observers. Some of these cases—a very small proportion surely—may have developed because of an inherited or family tendency.<sup>6</sup> Sutherland and Walker<sup>7</sup> report interstitial nephritis in infants, and refer to the fact that such nephritis due to syphilis is not unusual.

Carpenter<sup>8</sup> reviews the subject of nephritis in *infants*, and comes to the conclusion that infantile interstitial nephritis may be produced by toxins other than those of syphilis; possibly toxins of intestinal origin may be the cause in some cases. Occasionally from unknown cause an early arteriosclerosis develops, as in the case described by Egon Rach,<sup>9</sup> of a girl, aged thirteen years, in whom a chronic nephritis with dropsy was followed by hypertrophy of the left ventricle, rigid arteries, and death from cerebral hemorrhage.

*Gout* is a common cause of chronic nephritis. There is not such a unanimity in regarding *lead* as the exciting cause of chronic nephritis. Many are inclined to look upon the contracted kidney developing in the course of chronic lead poisoning as due rather to the gouty condition that is so often a sequel of lead poisoning ("lead gout"). Olliver, in 1863, described albuminuria in workers in lead. Since then numerous statistical studies have borne out the truth of this observation. Senator, Wagner, and Dickinson found many cases of contracted kidney among workers in lead. It would seem that lead alone without gout may produce chronic interstitial nephritis.

Of the influence of *alcohol* in the production of nephritis there is little doubt. But observers differ widely in their estimate as to the importance

<sup>1</sup> *Specielle Pathologie*, fourth edition, ii.

<sup>2</sup> *Practitioner*, 1887, xxix, 104.

<sup>3</sup> *Transactions of College of Physicians of Philadelphia*, 1883.

<sup>4</sup> *Ztschr. f. klin. Med.*, 38, 127, with literature.

<sup>5</sup> *Norsk. Mag. f. Lægevid.*, 1904, No. 8.

<sup>6</sup> Heubner. *Ueber chronische Nephritis und Albuminurie im Kindesalter*, Berlin, 1897.

<sup>7</sup> *Archives of Pediatrics*, 1903, xx, 288, also *British Medical Journal*, 1903, i, 959.

<sup>8</sup> *British Journal of Children's Diseases*, iv, 421.

<sup>9</sup> Abstract in *Deutsch. med. Woch.*, 1907, No. 34, p. 1387.



of alcohol as a causative agent. Thus of two French observers, Rayer placed alcohol at the head of the list of causes, while Lancereaux denies that alcohol is a common cause. Experimentally, little definite has been brought forth to show a direct influence of alcohol in the production of chronic interstitial nephritis. Clinically, the question is by no means settled. It would seem that alcohol is unquestionably an important factor in the production of chronic nephritis, not always through the direct action of the alcohol on the kidneys, but oftener indirectly through perversion of gastric and hepatic function, through induced faulty metabolism, through secondary digestive disorders, through exposures and excesses of various kinds, all the result of alcoholic overindulgence.

Not infrequently chronic interstitial nephritis can be traced to a preceding *acute infectious disease* that was complicated by acute nephritis. Many cases reported as due to the acute infectious disease are undoubtedly instances in which a previously existing but unsuspected nephritis has been noted only because of the urinary examination at the time of, or soon following, the infectious process. Slight attacks of tonsillitis may be a cause more often than we have generally supposed. Most of the cases of chronic interstitial nephritis seen in childhood are probably, as Heubner suggests, due to previous infections—scarlet fever, measles, angina, pneumonia, intestinal disturbances due to bacteria—which may have been slight in character and in which no symptoms drew attention to the urine or kidneys. In this connection one is led to think of the marked acute parenchymatous degeneration so frequently present in these acute infections, of the cellular destruction often seen in this condition and in acute nephritis, of the numerous patches of visceral round-celled infiltration and of focal necrosis, and to surmise that in place of the destroyed cell or in the area of focal necrosis fibrous tissue may be formed and serve as a nucleus for the spread of a local or more extensive fibrosis, in accordance with Weigert's law of primary destruction of specific tissue elements and replacement by newly formed connective tissue.

A cause whose influence it is impossible accurately to estimate and to which reference has been made in discussing the general etiology, is repeated or chronic *gastro-intestinal disturbances* with faulty digestion, and the still more obscure *faulty metabolism* on the part of such organs as the liver, pancreas, or adrenal. Unnatural chemical products may be present in the blood under these conditions, and be the irritating cause of the change in the kidney. In this way alcohol, by disturbing the function of stomach, bowel, and liver, may be an indirect cause of nephritis. So overeating, or the eating of rich or improper food, the excessive use of proteins, in short, any often-repeated dietetic errors, may be conceived of as the underlying causative factor in the production of chronic nephritis. How much influence disturbances in the function of the liver, pancreas, thyroid, or adrenal may have is not clear. Nephritis in connection with hepatic cirrhosis is not uncommon, both perhaps due to the same cause; yet the influence of perverted function of the liver on the kidney, forcing it to eliminate improperly elaborated substances,

is not to be underestimated. Caro<sup>1</sup> found nephritis in from five to eight days after experimental thyroidectomy in cats. Diabetics often have albuminuria and true chronic nephritis may develop, possibly from overwork of the kidney. The relation of renal sclerosis and of general arteriosclerosis to perverted adrenal function is still unknown. Many cases of chronic interstitial nephritis may then have their origin in undetected anatomical or physiological changes in other viscera.

The relative infrequency of this form of nephritis in the warmer climates has been frequently noted. This may be in a measure accounted for by the fact that in the warmer climate there is less exposure to cold, inclement weather, and sudden changes of temperature; the inhabitants consume less protein food, drink less strong alcoholic drinks, and are subjected to less wear and tear through the strenuous life.

The kidney of *pregnancy* may be the starting-point of the disease, although some cases regarded as originating during pregnancy have been cases of chronic nephritis, with an acute exacerbation.

*Cardiac disease* and chronic interstitial nephritis often coexist. The relation between the two diseases is not always clearly definable. In many instances the same cause has produced the nephritis and the valvular or myocardial lesion. In other cases a primary renal lesion has caused the secondary changes in the heart. In a few cases chronic interstitial changes in the kidney result from an incompetent heart, with its resulting long-standing passive congestion of the kidney (cyanotic induration), together with its accompanying toxic condition of the blood from cyanosis, alimentary disturbances, and faulty metabolism. Localized areas of chronic fibrosis in the kidney often result from renal infarcts that may have their origin in a diseased heart.

Since Gull and Sutton, over forty years ago, called attention to the fact that certain diseased conditions affected the entire vascular system as a unit, some cases of chronic disease of the kidney have been regarded as but part and parcel of general *arteriosclerosis*. The causes of the arteriosclerotic kidney would be those of arteriosclerosis in general: old age, heredity, syphilis, lead, gout, alcohol, excessive work, and preceding infectious diseases. Chronic interstitial nephritis is found oftener in males and in those past the age of thirty; the arteriosclerotic kidney, in the stricter sense, is rarely seen until after forty-five.

Chronic fibroid changes may take place in the kidney when there is *chronic obstruction* to the outflow of urine, or disease of the pelvis of the kidney. Thus, in stricture of the urethra or ureter, in cystitis and pyelitis this is at times noted. While not in a strict sense of the same type as chronic interstitial nephritis, this "consecutive nephritis" may be here referred to, as it is practically a fibrosis.

A *traumatic origin* of some cases of nephritis has been alleged. Küster, Edlefsen, Curschmann (the younger), Engel, Posner,<sup>2</sup> and others have written concerning it. Orth, in the discussion on Ponfick's and Müller's papers at the Congress in 1905, referred to specimens in his possession

<sup>1</sup> *Mitt. a. d. Grenz. d. Med. u. Chir.*, 1907, xvii, 447.

<sup>2</sup> *Deutsch. med. Woch.*, 1906, xxxii, No. 12, 454.

showing typical contracted kidney from subcutaneous injury of the kidney. Under trauma might also be included Newman's cases of nephritis in floating kidneys,<sup>1</sup> in which condition Newman finds Bright's disease not so very uncommon; and also some cases of obstruction to the ureter with resulting circulatory, nutritional, and fibrotic processes in the kidney. Tornellini<sup>2</sup> and Senator<sup>3</sup> have still further discussed the experimental and clinical features of traumatic chronic nephritis.

Many attempts have been made to produce *experimentally* a chronic nephritis of the type of the contracted kidney. These efforts have met with but indifferent success. The conclusions, too, in some instances are rather hastily drawn, the number of observations too few, and not enough consideration given to the fact that albuminuria and renal disease might have existed in the animals used prior to the experiments. In dogs chronic nephritis seems to be not uncommon.<sup>4</sup> The results that have been the most nearly constant in the way of a chronic nephritis, and not merely acute or chronic degenerative lesions or those of temporary character, have been brought about by the long-continued use of small doses of the salts of lead. Haven Emerson<sup>5</sup> has done suggestive, although not yet conclusive, work in attempting to produce chronic nephritis in dogs by using means that presumably materially alter the circulation in the kidney, and he argues in favor of circulatory stagnation and defective blood-supply to the kidney as potent causes of chronic nephritis, and as capable of being brought about by chemical or mechanical agents. But no experimental work can exactly or even approximately duplicate the conditions that seem operative in the production of chronic interstitial nephritis in man. The influence of heredity, dietetic errors, faults of metabolism, syphilis, many of the infections, the wear and tear of the strenuous life and of excessive mental and nervous strain—all these continuing perhaps for years—cannot be reproduced in experiments on the lower animals. Bradford<sup>6</sup> in his Croonian lectures on Bright's Disease and its Varieties, reviewed the experimental work on nephritis. While showing its great value, he says that there are still lacking many of the conditions found clinically, and that the results (*e. g.*, with nephrotoxins) are often far from conclusive.

After all is said concerning the etiology of chronic interstitial nephritis, we come back to Rosenstein's statement, already quoted, that for the majority of cases we cannot assign a definite cause. In many cases a combination of causes seems to operate. A peculiar susceptibility may explain why one individual will develop the disease, while another, under what seem to be exactly similar conditions, or even under conditions that would seem more likely to favor the development of nephritis, will escape.

<sup>1</sup> *Glasgow Medical Journal*, 1904.

<sup>2</sup> *Vierteljahrsscher. f. gerichtl. Med.*, Band xxxiv, Heft 1.

<sup>3</sup> Cf. Senator, *Berlin. klin. Woch.*, March 16, 1903; also Engel, *ibid.*, 1903, No. 10.

<sup>4</sup> Cf. Pearce, *Univ. Penn. Med. Bull.*, 1903-04, xvi, 217; also Ophüls, *Jour. Med. Research*, 1908, 49.

<sup>5</sup> *Arch. Int. Med.*, 1908, i, No. 5 (references to experimental nephritis). Cf. also O'Hare, *ibid.*, 1913, xii, 49.

<sup>6</sup> *London Lancet*, 1904, vol. ii.



**Pathological Anatomy.—Primary Chronic Interstitial Nephritis.**—Almost always the process is bilateral. There are probably occasional exceptions to this statement (Israel, Senator, Klemperer), and at the very beginning of an acute or even chronic nephritis it is not impossible that one kidney alone may for a short time be involved. But such labored arguments as those of Pousson,<sup>1</sup> striving to prove that unilateral nephritis *might* occur, and therefore does occur not infrequently, are more than offset by statements such as those of Guiteras, who in 500 autopsies on patients with Bright's disease never saw one kidney alone involved, or of Kümmell, who says that in the rich autopsy material at Hamburg no instance of unilateral nephritis has been seen.

The kidneys are small, sometimes unequally so. The single kidney may weigh only fifty or sixty grams, occasionally even less than this. The color is variable, but in general is red or grayish red. The fatty tissue about the kidney is unusually abundant and may be quite firmly adherent to the true fibrous capsule. This latter capsule is often quite vascular, and is thickened and raised in uneven manner by the granular elevations of the kidney surface beneath, that alternate irregularly with darker red depressed areas that denote underlying contracting fibrous tissue. When the capsule is stripped off, it is found to be adherent, especially over these depressed regions, and when it is forcibly removed more or less of kidney substance is pulled away with it, leaving a rough, granular, uneven, reddish surface that is quite characteristic. The kidney is hard and cuts with increased resistance. Small retention cysts may be numerous. The cysts usually contain a pale-yellow, serous, or urinous-looking fluid that is albuminous, perhaps slightly blood-stained, and contains more or less urea. The cut arteries may be plainly seen, and may gape and show thickened walls. The cortex is narrowed; it may measure only 1 mm. In some places the pyramids lie almost immediately under the capsule. The pyramids, although absolutely shrunken, seem by comparison with the contracted cortex to be large. The cut surface is reddish in color, with a liberal mottling of gray due to the abundant connective tissue. Beneath the depressed areas on the surface, with the naked eye or a low-power lens, may be seen masses of fibrous tissue often extending quite a distance into the kidney. The lighter areas that form the projections on the surface represent the more nearly normal tissue, some of which may be compensatorily hypertrophied. There is commonly an abundance of fat in the renal pelvis.

The microscope reveals a general increase in the fibrous tissue, a thickening of the vessel walls, destruction of glomeruli, and more or less degeneration of the renal epithelium. The cortex, especially the labyrinth, shows the most marked change, although the lesions are not uniform in their distribution. Even in the areas between the labyrinths that are more nearly normal the epithelium often shows some fatty degeneration, and foci of round-cell infiltration may give evidence of an early stage of the indurative process.

<sup>1</sup> *Zeitsch. f. Urologie*, 1907, i, 853.

*Malpighian Bodies.*—Many glomeruli are destroyed, being represented by structureless hyaline masses. Others show the remains of the capillary tufts in the shape of homogeneous or granular balls in which a few nuclei may still be seen. Again, the capillary tuft, the capsular space, and even the epithelium lining Bowman's capsule may appear normal, but a richly nuclear fibrous ring, often quite broad, surrounds the entire Malpighian body, or the ring may be dense and poor in nuclei.

The capsular space may be obliterated, the capillaries and capsule being adherent; or the space may be widened, the result of obstruction to the outflow of urine from obliterated tubules, the dilatation being on the order of a retention cyst. Compression of the tuft may thus result. Nuclear proliferation is often seen in the tuft. Especially in the small projections on the surface of the kidney that give it its granular appearance, large compensatorily hypertrophied Malpighian bodies may be seen showing little or no pathological changes. In places the bodies, from atrophy and contraction of intervening tissue, are closer together than in the normal kidney.

It is easy to understand how the glomerular function is seriously interfered with by these changes and how the structure and function of the tubular epithelium must be, in consequence altered. The glomerular lesion, however, is not necessarily primary. The more correct conception is to regard the process as from the first more or less diffuse, and to look upon a change in one part as necessarily leading to change in another, after the manner of the vicious circle.

*Tubules.*—Atrophy is more or less marked. Many tubules are narrow, lined with small flat or cubical cells, and quite collapsed. Others, from blocking of their excretory ducts, have become dilated with hyaline-looking or granular and fatty cells lining them, or have even formed retention cysts of various shapes and sizes. These cysts sometimes coalesce so as to resemble compound cysts. In some tubules all the cells have disappeared, leaving bare the basement membrane. In the areas that show compensatory hypertrophy, the tubules and cells at times seem larger than normal or even increased in number, reminding one of the somewhat similar, almost adenomatous increase of the healthy liver cells in hepatic cirrhosis.

*The Vessels.*—An endarteritis or even a mesarteritis can usually be made out, the intimal thickening often perceptibly narrowing the lumen. The smaller intertubular vessels are specially involved and are often entirely obliterated. This must, by causing interference with the blood-flow, increase the pressure in the glomerular capillaries. This has been given as one explanation of the polyuria of chronic interstitial nephritis.

The degree to which different arteries are altered varies, some showing marked thickening in the outer and middle coats, but especially in the subendothelial layer, others but slight changes. The sclerosis is sometimes patchy, even in the individual artery, one portion of the circumference showing an extensive lesion, while the remainder of the ring is nearly normal. The lumen of the thick-walled vessel may be nearly normal, the pipestem-like artery gaping with wideopen mouth as it is cut across, while in other vessels the caliber is gradually narrowed

until it is quite obliterated. Dickinson<sup>1</sup> found by actual measurements that the caliber of the primary arteries was not altered even though the walls were thick. The obstruction to circulation, as he proved, was in the minute arterioles and in the capillaries, many of which were entirely destroyed. The roughened intima with the sluggish current that must flow through some of these vessels favors thrombosis, and thrombi may be seen in some of the vessels, such as the smaller interlobular arteries. From destruction of vessels there results a compensatory collateral venous circulation. Part of the blood escapes by way of the vessels of the renal capsule and the perirenal fat.

*The Interstitial Tissue.*—This is increased. The thick, fibrous bands surrounding the Malpighian bodies present perhaps the most striking picture, but the newly formed connective tissue rich in nuclei, or the old scar-like bands and masses, may be seen nearly everywhere, between the tubules, in the pyramids, and about the vessels, and especially running down into the labyrinth from the surface depressions and sending out bands of fibrous tissue that encircle and ensnare the healthy tissue on either side. Masses of round cells representing young contractile tissue may be seen, especially under the capsule and around the glomeruli and vessels, from which points the process extends downward and out into the intertubular tissue. The contraction follows so soon that even though this nuclear overgrowth, as it has been termed, be excessive, the kidney is always small. In places, little or no relic of renal structure is to be made out, the section showing merely dense fibrous tissue. Sometimes calcification is found in this adventitious fibrous tissue.

**Secondary Contracted Kidney.**—This is seen in its earliest stage in some of the kidneys of chronic parenchymatous nephritis, the large white kidney, in which a few depressions on the surface and a beginning hardening from fibrosis show that had death been deferred for several months the kidney of secondary contraction would, in all probability, have been present. This kidney in reality seems much like a cross between the kidney of chronic parenchymatous nephritis and the contracted kidney. It is pale in color, of normal or diminished size, its capsule thick, the surface granular. The kidney feels firm to the touch. The cortex is narrow and pale. Fibrous tissue is seen in greater or less abundance, the glomeruli are in general small, surrounded by bands of fibrous tissue and at times have undergone atrophy and completely disappeared. Hyaline degeneration of the epithelium of the tubules is pronounced or the cells may have entirely disappeared, leaving the tubule denuded and seemingly dilated. The vessels may show mural thickening. The picture in advanced cases is not unlike that of the chronic interstitial nephritis. Bradford believes the contracted white kidney is a distinct entity and not related, on the one hand, to the large white kidney or, on the other, to the truly granular kidney.

**Arteriosclerotic Kidney.**—This form is a not uncommon postmortem finding in those past the middle years of life, and especially in those who have had operating upon them for many years the causes favoring

<sup>1</sup> *Lancet*, 1895, ii; also *Medico-Chirurgical Transactions*, vol. xliii.



the development of general arteriosclerosis. The arteriosclerotic kidney, as already stated, is generally but one manifestation of a widely distributed vascular sclerosis, so that at autopsy cardiac hypertrophy, thickened cerebral vessels, with perhaps rupture and hemorrhage, are commonly met with. The conception of the disease is that of a simple non-inflammatory atrophy. The kidney itself is usually reddish or grayish red in color, and but slightly smaller than normal. In long-standing cases, however, there may be extreme reduction in size. It is firm to the touch, and the capsule that is not much thickened may often be stripped off readily without bringing away much of the kidney substance. The surface of the kidney is smooth, although here and there the local cortical atrophy may be revealed by a depressed area, and the presence of cicatricial tissue in such an area will be shown not alone by the microscopic examination, but by the fact that the capsule is bound to the kidney at this point by fibrous adhesions. A few sub-capsular cysts are occasionally seen.

The hard cut surface may show gaping vessels; the cortex is narrow. Some of the changes seen on microscopic examination are in many respects similar to those described under primary chronic interstitial nephritis; and it is, in fact, difficult to differentiate between changes that are purely degenerative or atrophic and those that are inflammatory, or to tell which change is primary. Many of the smaller vessels show intimal thickening. The small-celled infiltration is, however, lacking or but slightly marked. There is less striated connective-tissue thickening about Bowman's capsule than in the inflammatory form. Many of the Malpighian bodies are destroyed. In others, the capillary tuft may be obscurely outlined as to its details, being represented by a homogeneous, hyaline mass, with a few scattered nuclei still visible. The capsule proper may be thickened; on its inner side it may be denuded of its epithelium, and it may even have contracted down so as to be in immediate touch with the tuft, the capsular space thus being obliterated. In this form of renal disease, as in most others, there is seen that remarkable irregularity in the distribution of the lesion—the "patchy" distribution. This may result in normal glomeruli being seen side by side with those quite markedly altered or even completely destroyed.

Many tubules will appear normal. In others, however, the atrophy is manifest in the small size of the cells, the loss of their normal markings, their flattened shape, or their total destruction. Often the narrowed tubule has collapsed, leaving a cord-like mass to represent it, or possibly a small retention cyst. These cysts may contain a clear fluid with masses of colloid-like material. The same colloid-like masses, occasionally a hyaline or granular cast or granular and fatty epithelial cells, may be found in some of the tubules.

Among findings in *other organs* that are met with quite regularly in chronic interstitial nephritis must be mentioned the *hypertrophy of the heart* and the *sclerosis of the arteries*. Left heart hypertrophy is the rule, and is always present before enlargement of the right ventricle. In advanced cases and especially in cases where dilatation of the left heart has occurred leading to mitral insufficiency, there may be right heart

enlargement, and the whole heart is truly bovine. The aorta and smaller vessels show more or less advanced sclerotic changes. Even when the aorta may not be markedly involved, the smaller arteries, *e. g.*, in the spleen, will usually exhibit some degree of thickening of their walls. Exceptionally, typical contracted kidney has been found unaccompanied by arteriosclerosis or cardiac hypertrophy. Roth<sup>1</sup> reports six such cases. Death was generally from uremia. In most of the cases blood-pressure had been low. The causes of these cardiovascular changes are discussed elsewhere.<sup>2</sup>

Such accidental or complicating conditions as cerebral hemorrhage or dropsical accumulations, where toward the last there has been cardiac insufficiency, are often seen. The alimentary tract is usually in a state of catarrhal inflammation, and uremic ulcers may be present. Devic and Charvet<sup>3</sup> reviewed the entire subject of *uremic ulcers* and found them to be present oftenest in the chronic interstitial nephritis especially when uremic symptoms are prominent. Dickinson's<sup>4</sup> lectures also contain a comprehensive discussion of these ulcers.

It will be in place to mention here some recent experimental work on the pathological anatomy of nephritis of which, while far from conclusive, is surely suggestive, and should arouse interest in further experimental work of this kind. Laederich<sup>5</sup> finds that not only in animals, which die as the result of a sudden suppression of renal function, as by operative removal of the kidneys, are *hepatic* lesions due to toxic degeneration regularly found, but in cases in which a gradual renal insufficiency is brought about, certain peculiar hepatic cellular changes are found (*état clair avec surcharge glycogénique*). This condition of renal insufficiency, if continued for a long period, finally leads to a periportal sclerosis. One sees, therefore, the interdependence of these two eliminating organs. The kidneys and the liver are closely related. Hepatic insufficiency can determine renal changes; experiment shows that renal insufficiency may induce reactions and lesions in the liver.

Beaujard,<sup>6</sup> in a critical review, describes the *suprarenal* lesions in nephritis, as found by several observers. Cortical hyperplasia is common in interstitial nephritis. One of three explanations is possible: (1) The suprarenal hyperplasia may be the cause of the hypertension and independent of the nephritis; (2) the suprarenal hyperplasia is the cause of the hypertension, but it is produced by the nephritis; (3) the suprarenal hyperplasia is a reaction to the chronic auto-intoxication provoked by the nephritis, along with hypertension, but is not the cause of the hypertension. Darré<sup>7</sup> shows experimentally that in chronic nephritis there is, apparently from resulting intoxication, hyperplasia of the cortical portion of the suprarenal gland, with an apparent increase in function. This function Darré regards as an antitoxic one. These observations do not settle the question as to a possible relation between

<sup>1</sup> *Virchows Archiv*, 1907, Band clxxxviii, 527.

<sup>2</sup> For a *resumé* of the subject see Senator, *Deutsch. med. Woch.*, 1903, xxix, p. 1.

<sup>3</sup> *Revue de Méd.*, 1903, xxiii.

<sup>4</sup> *Brit. Med. Jour.*, 1876, i.

<sup>5</sup> *Des Modifications du Foie consécutives aux Altérations Rénales*, Paris, 1907.

<sup>6</sup> *La Semaine Médicale*, 1907, No. 20.

<sup>7</sup> *De l'influence des altérations du rein sur les glandes surrénales*, Thèse de Paris, 1907.

the hypertension of nephritis and the suprarenal. The hypertensive element of the suprarenal is supposed to emanate from the medullary rather than from the cortical portion.

Wiesel,<sup>1</sup> however, has found medullary hyperplasia in the adrenal in a case of subacute nephritis. He does not, however, interpret this as necessarily the cause of hypertension, but rather as a possible result or concomitant of cardiac hypertrophy.

**Symptoms.**—Chronic interstitial nephritis is often entirely unsuspected until some sudden uremic outbreak, or perhaps an apoplectic seizure, leads to an examination of the urine; or the disease may be accidentally detected in the course of a life insurance examination, the applicant regarding himself as in perfectly good health and being entirely free from symptoms. On the other hand, the disease may, for a long time, be rich in symptoms and the cause of years of ill-health and semi-invalidism. There is no one type of the malady. The picture presented is a bizarre one and subject to great variations.

The *onset* is generally insidious, therefore the date of its inception is unknown. What may perhaps be called a typical case is seen in one of middle years, who begins to fail somewhat in strength, is annoyed by headache or dizziness, has anorexia and other dyspeptic symptoms. Possibly he has noted a little polyuria, and has remarked that he is obliged to rise frequently at night to empty the bladder. For these rather indefinite symptoms he consults a physician, who finds him slightly anemic, with a heart enlarged, with blood-pressure high, and with the urine increased in amount, of low specific gravity, and containing a trace of albumin with a few casts. Possibly at this time retinal changes may be noted. Edema is conspicuously absent. The disease, however, in spite of care on the part of the physician and the patient, makes steady, although perhaps very slow, progress, with many ups and downs. Later, evidence of cardiac incompetence is manifested, with the usual dyspnoea, palpitation and oedema; this failure on the part of the heart, uremia, or possibly cerebral hemorrhage, may be the cause of death. But as has been said, there are many variations, and with the multiform manifestations of uremia, the numerous sequelæ of cardiovascular incompetence, the frequent intrusion of complicating maladies, the possible combinations are almost numberless, so that any clear-cut clinical picture of the disease cannot be drawn. The conditions that stand out most prominently and that form the basis of the diagnosis are the cardiovascular changes, the urinary findings, and the uremic manifestations.

**The Urine.**—Just when the urinary changes begin to manifest themselves is seldom definitely known, but by the time a diagnosis of the disease is possible the urine, as a rule, shows the following characteristics: It is increased in amount, from 2000 to 4000 cc. being commonly passed in twenty-four hours, although much larger amounts are not infrequently seen. The nocturnal urine is often greatly increased in amount. Even before polyuria is manifest, frequency of urination may be noted. To this frequent urination Dieulafoy has given the name pollakiuria, and

<sup>1</sup> *Wiener med. Woch.*, March 30, 1907.



he believes that it often precedes a polyuria. He further says that this pollakiuria is sometimes, particularly in women, or where it is a late manifestation, attended with considerable pain. As a rule, when there is an increased amount of urine, together with an increase in the frequency of micturition, the amount passed with each emptying of the bladder is considerable, although in some instances the product of each micturition is no more than is usual, or it may be even rather small in amount. Such frequency of urination is often noted at night, and when it occurs in a man beyond middle years may be wrongly looked upon as due to irritation from an enlarged prostate gland.

The urine is light in color, slightly acid in reaction, and the specific gravity less than normal. Specific gravities of 1005 to 1015 are very common. This low specific gravity, as Traube demonstrates, is not influenced so much by profuse sweating, diarrhoea, and vomiting as is the urine of health. Seldom even when congestion is added by reason of a weak heart has the urine a specific gravity over 1016, is it dark colored, or has it a rich sediment of salts (Stern). The total amount of solids for the twenty-four hours may be practically normal. The percentage of solids, in a single specimen, is naturally low. When the heart fails, and blood-pressure is lowered, the total amount of urine is usually diminished, and with this there is a decrease in the total amount of solids. The sediment, even when the urine has stood for a long time or has been centrifuged, is quite scanty. In this sediment a few crystals of calcium oxalate or of uric acid may be found. Examination also shows a few epithelial cells, a few hyaline or granular casts of varying size, and an occasional leukocyte, many being lymphocytes,<sup>1</sup> with perhaps a few stray red-blood corpuscles.

The amount of *blood*, however, may be much greater. Larger amounts of blood occur with an acute exacerbation. Sometimes a tendency to recurrence of hemorrhages is seen. The exact relation of some cases of so-called essential hemorrhage from the kidney, or renal hemophilia, to chronic nephritis is not clear. Israel<sup>2</sup> and Askanazy<sup>3</sup> think paroxysmal congestive attacks will often explain it. Kusomoto<sup>4</sup> finds rupture of vessels in the renal pelvis as the cause. Many writers of late believe not a few of the supposedly essential hemorrhages—hemorrhages without anatomical lesion—would prove to be, if studied more carefully as to cardiovascular findings, retina, casts, and the subsequent history, instances of chronic nephritis. Many such hemorrhages are from one kidney, and cease under nephrotomy.<sup>5</sup> Kapsammer<sup>6</sup> also speaks emphatically against an essential hematuria; there is always some lesion, he says, often a chronic nephritis.

There is no question that occasionally patients with chronic interstitial

<sup>1</sup> Cf. Senator, *Virchows Archiv*, Band exxi; also Schnütgen, *Berliner klin. Woch.*, 1907, No. 45.

<sup>2</sup> *Mill. a. d. Grenz. d. Med. u Chir.*, 1900, 471; also *Deutsch. med. Woch.*, 1902, No. 9.

<sup>3</sup> *Zeit. f. klin. Med.*, 1906, lviii, 145.

<sup>4</sup> *Deutsch. Arch. f. klin. Med.*, lxxxix, 405.

<sup>5</sup> Cf. H. A. Fowler, *New York Medical Journal*, November 25 and December 2, 1905, with extensive bibliography.

<sup>6</sup> *Nierendagnostik und Nierenchirurgie*, Wien, 1907, ii, 338

nephritis pass urine which is free from albumin. Postmortem, the renal lesion may be sufficiently distinct, yet no albumin and no dropsy have been noted during life (Stewart). These cases are, however, quite rare, and many of the instances in which chronic interstitial nephritis has been diagnosed, but no albumin found in the urine, are cases of arteriosclerotic kidney. Yet in some patients who have unmistakable primary chronic interstitial nephritis albumin may be absent after periods of prolonged rest, as, for instance, in the urine passed on first rising in the morning. Nearly always there is serum albumin, very often but a faint trace. The total amount for twenty-four hours is usually from one to five grams. Later in the history of the disease, and particularly when there is beginning failure on the part of the heart, the amount of albumin is decidedly greater, and in many instances the amount varies very much, being greater when there has been overeating, undue excitement, exposure to cold, etc.; and with exacerbations the amount of albumin will very materially increase. So, too, the albumin is often very considerable because the case is, as has already been stated, rather one of chronic diffuse nephritis than in the stricter sense one of the interstitial variety. Albumose is occasionally present in considerable amounts. The exact significance of this is not clear. It is said in some instances to precede the appearance of albumin in the urine in chronic nephritis. The molecular concentration of the urine is diminished; the freezing-point is, therefore, nearer 0° C. than normal.

In the arteriosclerotic kidney the urine may be free from albumin or show albumin only occasionally. The urine is, however, usually increased in amount, with the specific gravity nearly normal or slightly less than normal. With the centrifuge a few casts can usually be found. Excess in food, exposure to cold, overindulgence in drink, may cause an increase in the casts and a small amount of albumin to appear in the urine.

**Cardiovascular Changes.**—The exact time at which the changes in the heart and vessels begin is seldom known in a given case. Senator is firm in his belief that he has seen albumin in the urine with polyuria for a long time before cardiovascular changes have made their appearance. In practice, however, it is a rare thing to find a case of chronic interstitial nephritis permitting of diagnosis in which the cardiovascular changes are not more or less well pronounced. The importance of recognizing these changes cannot be overestimated. It has frequently been said, and with much truth, that the cardiovascular changes in chronic interstitial nephritis are of fully as much importance from the standpoint of diagnosis as the study of the urine.

The *heart* is increased in size and may be truly "bovine." The enlargement is chiefly in the left ventricle, the apex being displaced downward and to the left. The right heart may be pushed to the right so as to simulate enlargement, or later there may be a real enlargement of the right ventricle, that is, a general cardiac hypertrophy. False conclusions may sometimes be reached as to the existence of cardiac hypertrophy because of emphysema, which may conceal the true size of the heart. The apex impulse is usually strong, rather diffuse, and heaving. The first sound at the apex may be loud and booming, although

it is sometimes muffled. The closure of the aortic valves is accompanied by an accentuated, ringing tone, and the shock of the closure may often be palpated. With the greatly enlarged heart the point of maximum intensity of the aortic closure sound is often a little lower down and closer to the midsternum or even to the left sternal border than is normal. In many cases the loud, ringing, aortic closure is quite plainly heard at the apex. All these signs undergo many modifications when dilatation has occurred. Then the impulse of the heart may be feeble and wavy; the murmur of mitral regurgitation develops at the apex; gallop rhythm, doubling of the first tone, embryocardia, extrasystole, may also appear, and naturally dyspnœa, cyanosis, and dropsy are also manifest. In fact, a difficult problem is presented to the physician, if he happens to see the patient for the first time late in the course of a chronic interstitial nephritis, to tell whether the disease is primarily cardiac or renal. At this time a presystolic murmur somewhat like that of mitral stenosis is said by Bradford to be present.

The peripheral vessels generally show changes. The arteries are tortuous and the walls frequently thickened. The blood-pressure is increased and the tension is high. The pulse may have a hard, incompressible, cord-like feel. It is difficult to estimate accurately the blood-pressure by the finger alone, as is proved by the use of the sphygmomanometer. Systolic blood-pressures in chronic interstitial nephritis are very frequently over 170 mm. Hg., and in the more serious cases and late in the history of the disease the pressure rises to 220 or even considerably over this. Sphygmographic tracings generally show a rather gradual ascent and a blunt or square apex. With a failure of the heart there is naturally a fall in blood-pressure. The pulse under these circumstances will be smaller and is frequently irregular. Some phenomena of nephritis depend in part, at least, on this high blood-pressure, on the hypertrophy of the heart and the degenerative changes that have taken place in the vessels. Among these might be mentioned headache, dizziness, and hemorrhages.

**Uremia.**—For many of the phenomena of chronic interstitial nephritis an explanation is offered by *uremia*. These toxic symptoms may be mild and of long standing, the so-called chronic uremia; or they may be brusque in their onset and malignant in their severity, as in sudden severe headaches, convulsions, and fatal coma, the acute uremia; though there is no special gain from the attempt to draw a very sharp—an artificially sharp—line between the acute and chronic uremic phenomena.

One hardly knows where to begin the description, for in practice patients come to the physician with a most promiscuous variety of complaints, one organ or system of organs showing perversion of function in one individual, another in other. One patient consults his physician because of dyspepsia, or it may be for pruritus, poor vision, headaches, dizziness, diarrhœa, cough, dyspnœa, or nosebleed. Many come because they are "run down." They have lost in vitality, lack energy, seem listless, cannot endure physical or mental strain as formerly, and have lost in weight. This condition, due to chronic intoxication, is revealed



not alone by these subjective complaints but by the examination of the patient. He appears worn, tired, often anxious. He shows some emaciation. His color is pale or sallow, at times cachectic enough to make one fear the existence of a malignant growth.

The *blood* shows an anemia of the secondary type, and the hemoglobin is often around 60 to 70 per cent. Hydremia is rarely present during the earlier stages of this form of nephritis, as in other forms of Bright's disease, and the specific gravity of the blood will be nearly normal. Late in the disease, when the heart has failed, the blood condition is more of a mixture of anemia, hydremia, and cyanosis. The freezing-point of the blood is generally normal,  $-0.57^{\circ}$  C., until late, when severer uremic symptoms appear; then it is lower,  $-0.59^{\circ}$  or  $-0.61^{\circ}$  C. The blood contains a pressor substance regarded by some—Schur and Wiesel,<sup>1</sup> Ehrmann<sup>2</sup>—as adrenalin, though Schlayer<sup>3</sup> says more proof must be offered that the substance in the blood with the hypertensive and mydriatic qualities is really adrenalin, and brings forward some experimental work that seems to go far toward disproving the identity of this substance and adrenalin. In the later stages of the disease, when the patient has suffered for a long time from gastro-intestinal disturbance, such as nausea and vomiting, from dyspnoea, pain and loss of sleep, and when the heart's action is poor, the evidence of malnutrition is often very pronounced, and the sallow, haggard, emaciated, bedridden patient, with his anxious look, dyspnoea, tortuous, visibly beating temporals, makes a picture showing the ravages of a disease as relentless in its progress and as destructive of health as carcinoma or tuberculosis. And yet it is remarkable how, early in the disease, many persons, and especially adults, may for years preserve an outward appearance of health, florid countenance, with firm musculature, springy step, and active mentality. Some are plethoric and corpulent.

*Digestive disturbances* sooner or later make their appearance. A loss of appetite, distress after eating, flatulence, coated tongue, occasional feelings of nausea, are common complaints even early in the course of the disease. Later, all these symptoms become aggravated. At times vomiting may come on in a manner almost explosive, much as in cases of cerebral disease, and in some instances it may be a question how much of the nausea and vomiting is due to central irritation, "nervous vomiting," so-called, and how much is due to a local condition of chronic gastritis that so often accompanies a nephritis, or to local irritation from the attempt on the part of the body to eliminate urea or its decomposition products, and perhaps other urinary constituents through the avenue of the stomach, *i. e.*, vicariously, for the kidney. Epigastric pain may be complained of; hiccough may be annoying. At times a severe stomatitis is seen, and salivation is sometimes disturbing. Thirst may be extreme, especially when there is marked polyuria. The fetid odor to the breath is at times so pronounced and so characteristically urinous (ammoniacal; trimethylamin, Senator) as to be of suggestive

<sup>1</sup> *Wiener klin. Woch.*, 1907, No. 23.

<sup>2</sup> *Archiv f. exper. Pathol.*, Band liii.

<sup>3</sup> *Deutsch. med. Woch.*, November 14, 1907.

help in diagnosis. It is usually an indication of extreme toxemia and is of bad prognostic import.

The *bowels* may be constipated or may continue regular. Yet looseness of the bowels is apt to occur as a sequel to the faulty gastric digestion just mentioned. Diarrhœa independently of a disordered stomach may be annoying and weakening. Diarrhœa in general is to be regarded as due to toxemia, to the chronic catarrhal inflammation of the mucosa so common in nephritis, as secondary to gastric disturbance, or as the result of local irritation due to efforts at vicarious elimination on the part of the intestine. At times the stools are more frequent at night than during the day. The presence in the intestine of the so-called uremic ulcer may explain an intractable nephritic diarrhœa.

*Respiratory symptoms* are not infrequent. Catarrhal bronchitis is common, with exacerbations in cold weather and with failing heart.

*Dyspnœa* in contracted kidney is common, although the pathogenesis is by no means simple. In some instances a more or less continuous dyspnœa is present, yet aggravated by exertion, seemingly a dyspnœa partly uremic, yet in a measure cardiac. Again, it seems wholly cardiac, and is noted only on exertion, the heart being incompetent when any unusual demand is made upon it. Most characteristic, however, is a dyspnœa that is paroxysmal and very often nocturnal. The sufferer is awakened with a feeling of oppression and weight in the chest, sometimes a distress that is painful and almost anginal in nature. He sits up in bed and leans forward, in order to breathe the more easily. His labored breathing is as in asthma, the piping and whistling sounds being made out on thoracic auscultation, or even heard at a distance. The attack may be over in a few minutes, to be repeated later in the night. Sometimes relief comes with the raising of thick mucus or a thinner watery fluid from the bronchi. What part is played by the heart in these cases, what by spasm of the bronchioles excited by toxins, what by the central nervous system irritated by the uremic poison, is not clear. It is often spoken of as a "cardiac asthma," occurring in the course of chronic interstitial nephritis when the heart is on the verge of failing. But the uremic element cannot be eliminated in many cases.

Somewhat resembling the asthma-like paroxysms and sometimes complicating them is a sudden acute œdema of the lungs. Dyspnœa is extreme, cyanosis is marked, and the pulse may grow feeble. The chest shows fine and coarse râles of every description, although chiefly of the moist variety. There is a persistent cough and an abundant, foamy, serous sputum, often bloody. In how far this condition is congestive and due to a weak heart, how far uremic-toxic or even inflammatory, is not clear. It is at times a serious condition and may be an immediate cause of death. An acute œdema of the glottis may also occur, even when œdema is not present in other parts of the body. This may be so threatening as to demand tracheotomy or other radical measures for prompt relief, failing which, death may be caused by suffocation.

When other symptoms of uremia are marked, as when the patient is stupid or even comatose, Cheyne-Stokes respiration is often present. But it may also be noted at times when the severer uremic symptoms

seem remote. The patient may be feeling fairly well and engaged in his regular occupation. The heart muscle, too, may be doing what seems to be good and efficient work, yet breathing of this type may be present. At times it may precede a fatal result by many months; it may even be present for a time and disappear. It is often a cause of no inconvenience to the patient; in other cases the periodicity is strikingly apparent to the patient, and the deep respirations are quite annoying.

Among causes of dyspnoea should, of course, be mentioned such conditions as complicating pneumonia or pleurisy. An insidious hydrothorax, too, is readily overlooked. This, especially if bilateral, is often a cause of dyspnoea; if not the sole cause, at least an auxiliary one. It is astonishing how, in some instances, the dyspnoea that has been explained and treated on the supposition that it was purely uremic, cardiac, or central, disappears when the transudate is removed. Pericarditis or hydropericardium is an occasional cause of dyspnoea.

*Hemorrhages* from the larynx or bronchi may occur, and these may be but one manifestation of a tendency to bleeding that is more or less widespread in this disease. In some instances a genuine hemorrhagic diathesis seems to develop, with bleeding from the gums, into and under the skin (purpura), and from various mucous membranes. Oftener, however, the hemorrhage does not seem to depend so much on a general blood-change as upon the degenerative alterations of the walls of the smaller vessels. Rupture of cerebral vessels is common in contracted kidney, a goodly percentage of cases of cerebral hemorrhage being due primarily to an underlying nephritis. This may occur even in the young nephritic.

*Nosebleed* is very common, and when not clearly explicable on other grounds should always lead to an investigation as to possible nephritis. It may be slight and oft-recurring. Yet it may be severe enough to demand plugging the posterior nares. Strümpell and Senator have each seen two fatalities from this form of hemorrhage. Hemorrhage from the stomach, the bowel, the uterus, the kidney, may occur. Hemorrhage into the tympanic cavity or into the membrana tympani may cause deafness; and retinal hemorrhage may cause disturbance of vision. These various hemorrhages, while commoner in advanced chronic interstitial nephritis, may be among the early symptoms.

The *skin* shows no characteristic features. Frequently it is dry and may occasionally be the seat of various lesions, eczema of various types being the one most frequently encountered. Itching is sometimes complained of, and is to be regarded as of toxic origin, comparable to the pruritus of diabetes, jaundice, and Graves' disease. At times the itching may be noted early, and it may be so severe as to reach the dignity of a serious complication, especially because of its interfering with sleep.

*Pigmentation* in nephritis, other than the sallow, cachectic hue already described, is relatively rare. Deposits of urea on the skin have been from time to time reported. Bartels<sup>1</sup> saw the hairs of the beard covered with crystals of urea. In another instance, two days before death, he saw the face and the skin of the trunk covered with the same crystals.

<sup>1</sup> *Ziemssen's Encyclopedia*, American translation, xv, 430.



A sensitiveness to cold (cryesthesia) is regarded by some as unusually common in nephritis. So also the paresthesias described as tingling and numbness, especially in the fingers and toes ("dead fingers," *doigt mort*), are often present in this disease. They are not, however, peculiar to it, being seen in other anemic, cachectic states.

The *rarity of œdema* in chronic interstitial nephritis has been mentioned. The œdema of cardiac incompetence very often appears late in the disease. Not infrequently one sees a case that is clearly of the type of the chronic interstitial variety in all respects save perhaps a little œdema, yet there is this one indication that the pathological process in the kidney is, after all, a diffuse one. Œdema in contracted kidney may be due also to an acute or subacute exacerbation of the nephritis.

The *nervous symptoms* in chronic interstitial nephritis are in number legion, in their variety protean. Nearly all of them may, however, be regarded as toxic or hemorrhagic. The chronic degenerative and sclerotic lesions of the central nervous system are seen with comparative rarity, and acute inflammatory processes are due to complications.

The symptoms of *toxemia* may show themselves in mild manner and for months or years, their manifestations being so slight and the increase in severity so gradual that the patient is hardly aware of the fact that he is in ill health. Yet on analysis of the testimony of the patient and his observing friends it will often be found that for some time there have been noted an easy mental fatigue, a lack of power of concentration and of the former quick grasp of business affairs; sleep may be poor, or the patient is drowsy during the day. He wakes in the morning with a headache, is annoyed at times by a full feeling in the head or by transient dizziness. He grows irritable or morose. He tries dieting, takes a short vacation, uses laxatives and tonics, but obtains only temporary relief. During the further course of the disease these symptoms may become more pronounced. Conditions of semi-stupor may be present for days, or there may be periods of excitement. While delirium and mania are oftener seen late in the disease, they occasionally break forth rather abruptly when the patient seems to be doing well, or possibly before the individual regards himself as a patient, before he has noted symptoms of gravity sufficient to induce him to consult a physician. Delusional insanity (*folie Brightique*) is occasionally met with, and the delusions, *e. g.*, of persecution, may be so extreme as to make it necessary to place the patient under restraint in an asylum. True melancholia is not encountered so often.

Many nephritics are great sufferers from *pain*. Pain in the back, popularly regarded as so frequently an indication of Bright's disease, is a very rare complaint. A rare occurrence is colicky pain in the renal region often radiating along the ureter, as in true calculous renal colic, and accompanied by hemorrhage, often profuse. Blood-clots passing down the ureter explain the pain in some cases. In others, the explanation is probably that of Israel and of Askanazy, that both the hemorrhage and the colicky pain are to be ascribed to paroxysmal congestion.

*Neuralgias* in the peripheral nerves may be the cause of pain, and peripheral neuritis is sometimes clearly demonstrable in these cases.

But the most frequent form of nephritic pain is *headache*. It may come on insidiously, but the attacks of pain grow more severe and more frequent. It may be like migraine in its periodicity and its hemicranial limitation. It is variously described by patients both as to its location and its character. The *resemblance to cerebral tumor* in some instances is worth noting. The severe headache, accompanied as it often is with nausea, vomiting, dizziness, and perhaps some mental disturbance, may resemble the symptom-complex of tumor of the brain, especially when an inflamed and swollen optic disk is discovered.

*Headache* is such an ordinary every-day occurrence that familiarity breeds contempt concerning it. No persistent headache should pass without a careful urinalysis, and one should be especially suspicious of those headaches that make their first appearance at about the age of forty years, and suspicious also of a sick headache that, instead of growing better at about the age of forty-five years, continues with its old severity or even grows worse. The headaches of nephritis go far to explain the loss of sleep and irritability in some of these sufferers.

The paresthetic sensations sometimes described have been mentioned in discussing the cutaneous manifestations—the dead fingers, the itching, cryesthesia either on contact or without, a sense of an “electric shock” especially just as one is falling off to sleep. *Cramps in the muscles*, especially those of the calf of the leg, are often annoying. At times the frequent recurrence of these cramps and their painful character seriously interfere with sleep, for they are prone to appear at night.

The so-called uremic *palsies* are pareses or paralyzes that may resemble, in their sudden onset and involvement of one-half the body, a hemiplegia from hemorrhage. But the paralysis is more commonly short-lived, lasting perhaps but a few seconds, minutes, or hours, and it usually is much more limited than to one-half the body, involving only an arm, a leg, or one side of the face. Transient aphasia is noted occasionally, or a deafness, or diplopia due to paralysis of some of the ocular muscles. These are comparable to the sudden transient blindness, the uremic amaurosis, and like it are central in origin, due to local cerebral oedema, or local concentration of the action of toxins on some motor centre, with temporary loss of function of a limited area of the brain. Minute hemorrhages or areas of acute softening may explain some of these cases.

Why *uremic convulsions* sometimes occur in such a sudden manner, unheralded by warning symptoms, is not clear. Apparently there is a cumulative action of the toxin, as is seen in the case of certain drugs; similar cumulative action is seen in lead poisoning. Usually premonition of trouble is given by severe headache, vertigo, nausea, dimness of vision, epigastric pain, and perhaps a rise in blood-pressure. The patellar reflex is generally exaggerated under these circumstances.<sup>1</sup>

When a convulsion occurs there is seldom any aura, as in epilepsy, nor is there the cry so often heard in that disease. The eyes roll upward and usually to one side, the pupils dilate, and for a moment the patient seems gazing with a fixed stare into distance. Then a jerking of the angles

<sup>1</sup> Lion, *Zeit. f. klin. Med.*, 1, 257, and Stevens, *British Medical Journal*, 1904, ii

of the mouth is seen, the head draws to one side, the muscles of the face and neck become clonically convulsed, the fingers and arms are flexed and likewise convulsed, and soon the entire musculature of the body is in irregular, jerky, violent motions. The face becomes livid or purple; foamy saliva issues from the mouth, and it may be streaked with blood that comes from a bitten tongue. The pulse grows rapid and weak, perhaps irregular, during the seizure. There may be involuntary evacuation of urine and feces. A few seconds or minutes are consumed by the attack, which ends with a quieting of the muscular spasm, a deep-drawn inspiration, and a rather prompt recovery of consciousness. If, however, the patient has been in a stupor or coma preceding the convulsion, or if the attacks are frequently repeated, sleep, stupor, or deep coma will follow. Usually the patient is somewhat dazed for a time, and knows little more of the attack than that "something has happened." When attacks are repeated at short intervals the temperature often rises and preagonal temperatures of 105° F. or over are not unusual. The pulse, after frequently repeated convulsions, becomes rapid and weak.

Convulsive seizures, in which the cerebral irritation is localized and the spasms of the Jacksonian type, are sometimes seen. Often slight jerking or twitching of the muscles may be noticed, and may be the cause of considerable annoyance to the patient, who tries to keep the muscles still. Nystagmus, local tremor, local clonic muscular contractions are sometimes apparently due to this same local cerebral irritation. Death may occur in coma without convulsive seizures. Oftener coma is preceded by convulsions or by the long train of symptoms that make up the dismal picture of chronic uremia, months or years of malaise, loss of strength, dyspepsia, headache, recurrent vomiting, *fetor ex ore*, insomnia, dyspnoea, epistaxis, polyuria, mental depression, the gradual cutting off of one business care after another, semi-invalidism, confinement to the house, then to the chair, and finally to the bed. Coma coming on under these circumstances is usually fatal.

The *special sense organs* may show anatomical changes or disturbances of function, none of which, however, may be called really characteristic except those of the eye. Taste is at times perverted, but seldom more so than in other severe intoxications. A loathing for food, a coated tongue, a fetid breath, are often coupled with the statement on the part of the patient that "food does not taste good" or things taste wrong. Complaints are occasionally heard of inability to smell or of disagreeable odors when none are about.

*Hearing* is usually good. But there is often a ringing in the ears that is out of all proportion to the degree of anemia present, and that is to be viewed as toxic. Deafness, partial and transitory, may occur, comparable to the amaurosis and uremic palsies, and apparently due to disturbance of the auditory centres. Hemorrhage into the middle or inner ear is occasionally the cause of deafness, and a vertigo resembling that of Ménière's disease has been described (*vertigo Brightique*).

The *ocular* manifestations of chronic interstitial nephritis are common. For this reason and because of certain features that are peculiar, they deserve to be considered from the point of view of diagnosis as of the



first rank. Often, indeed, the diagnosis of this form of renal disease is first made by the oculist, or the crucial test is the finding on examination of the eye. While the retinal changes are the most characteristic, other subjective and objective symptoms are worthy of note.

The *amaurosis* comes on, as a rule, suddenly, may be complete or partial, is bilateral and commonly transitory, lasting but a few minutes, or at most a few hours. Retinal examination in these cases shows nothing to explain the blindness which is central in origin.

*Diplopia* due to uremic palsy of some of the ocular muscles is occasionally seen. So, too, are conjunctival and palpebral hemorrhage. While oedema is not at all characteristic of this particular form of nephritis, the watery eye, "Bright's eye," so-called, may be observed. Exophthalmic prominence of the eyeball—unilateral or bilateral—is comparatively common. Insufficiency of the external muscles of the eye, emaciation of structures about the eye, undue fulness of the retrobulbar vessels, or rarely a hemorrhage in the orbit help to explain it.

*Retinal changes* may produce no disturbance of vision that attracts the attention of the patient, and are only discovered as the result of routine examination. On the other hand, the lesion of the retina may be manifest by marked and sometimes early symptoms. It is particularly in patients of this class that the diagnosis of nephritis is made by the oculist, who is consulted before the physician. In rare instances these ocular lesions have been found before the urinary evidences of a chronic nephritis can be made out. The symptoms will naturally vary much with the extent to which the retina is involved, and especially with the damage wrought in the macular region. Dimness of vision, blurring of the outlines of objects seen, an appearance of a mist or veil before the eyes are often described. Blind spots may cause the patient unconsciously to turn the head to one side or the other, so that the light from the object looked at may strike the healthy, undamaged part of the retina, or he may be conscious of his ability to see much more clearly objects located in one position than in another, realizing that he has some defect in eyesight. These retinal changes are much rarer in the acute or chronic parenchymatous form, and in amyloid kidney unassociated with chronic indurative processes they are probably not found. With the kidney of pregnancy, especially when it is of rather long standing, they are not uncommon. Retinal hemorrhages, too, are found in the eyes of those with general arteriosclerosis, where the lesion is to be viewed as but one of the consequences of the general vascular disease.

For the rarer changes and for minuter details concerning the retina in nephritis, works on ophthalmology should be consulted. Aid must frequently be asked of the ophthalmologist in the interpretation of ocular symptoms and findings in chronic nephritis.

The commoner changes in the retina of Bright's disease are whitish or yellowish patches, hemorrhages, diffuse retinal opacity from oedema, optic papillitis, diffused retinitis, atrophic changes consecutive to inflammation. Of these six changes enumerated by Gowers, the first three are common. Tirard would add to the last three the more uncommon,

the occasional occurrence of extensive retinal detachment, which, of course, seriously impairs vision.

No appearance is more strikingly peculiar than the yellowish or white spots that are seen about the disk and macula or scattered more widely throughout the retina. The spots may be but minute, glistening dots, or they may be larger and represent the fusion of several smaller ones. Spots as large as the disk may be seen; these larger ones are more apt to be located near the disk, and are thought by some to represent a more advanced stage of the degenerative process. Most characteristic is the grouping of small spots about the macula as a centre from which they radiate, fan-like, in every direction, each ray being made up of a succession of these whitish areas arranged as a broken line. The macula may appear dark red. At times the whitish areas are scattered so freely throughout the retina as to present an appearance as though one had with a fine brush spattered white enamel paint over its surface.

*Hemorrhagic extravasations* are often present, sometimes with and sometimes without the whitish areas. These may be minute dots, larger irregular patches, or lines and streaks of blood running beside the vessel. They are sometimes "flame-shaped." These hemorrhages are more apt to occur in renal disease associated with marked arteriosclerosis, yet they are often found in cases of primary chronic interstitial nephritis where the sclerosis may be insignificant. The retinal changes of chronic nephritis are commonly bilateral.

In some of these cases the veins are distended, especially distally to the point where an artery crosses a vein. These tortuous and distended veins are seen also in the cases where there is a neuritis or a neuroretinitis. Here the disk is usually slightly reddened and a trifle swollen, or it is greatly swollen and its outlines and all its details obscured. The arteries are small. Grayish and whitish streaks run out from the disk, the contour of the vessels often being lost at this point. Hemorrhages near the vessels, close to or at a distance from the disk, may be seen. The retina may appear slightly cloudy.

The essential nature of each of these retinal lesions is not entirely clear, although they seem dependent on the degenerative changes in the vessels, the high blood-pressure, and perhaps upon the toxemic condition, or even in a measure upon the general malnutrition of the advanced nephritic. They are generally regarded as degenerative rather than inflammatory. These changes in the retina, often collectively referred to as *albuminuric retinitis*, are seen far oftener in advanced cases when vascular degenerative, perhaps markedly sclerotic, changes are pronounced, blood-pressure high, and toxemia clearly manifest. They are rightly looked upon as of bad prognostic import. The observation that patients seldom live more than two years from the time albuminuric retinitis is discovered has been abundantly confirmed, although there are exceptions to this rule.

It must not be forgotten that retinal appearances much like those seen in Bright's disease may be seen under other circumstances. The swollen disk of brain tumor, meningitis, and other intracranial lesions, as well as of severe anemias, lead poisoning, etc., must be kept in mind,

Nor must it be overlooked that hemorrhages may often be seen with the ophthalmoscope in pernicious anemia, leukemia, ulcerative endocarditis, sepsis, the so-called hemorrhagic or purpuric diseases, etc.

Care must therefore be exercised in the interpretation of the retinal condition, and while some of the retinal appearances are almost pathognomonic, the safer way is to reach a conclusion as to the existence of nephritis only after a comparison with the other subjective and objective findings, *i. e.*, to make albuminuric retinitis, like albuminuria and cardiac hypertrophy, take its place as a confirmatory sign in the symptom-complex rather than as an essentially pathognomonic sign.

**Complications.**—In the strictest sense, cardiac incompetence and dilatation may be regarded as the natural sequences of chronic interstitial nephritis. But the failing heart so often dominates the picture and so modifies the course of the disease as to justify its being looked upon as a complication. True valvular disease from preceding endocarditis or sclerotic process is, of course, a complication in the narrower sense of the term. In its effects upon the nephritis it is practically identical with the secondary dilatation. The basis of the cardiac weakness is the exhaustion of the myocardium, which in many instances shows fibrosis, largely the result of nutritional disturbances due to sclerosed coronary vessels.

Whether or not such gross or microscopic change in the heart muscle can be made out, the heart, although enlarged, finally from overwork shows signs of weakness. Dyspnoea is marked upon even slight exertion; it may be of the nocturnal asthmatic type already described. There is an annoying cough, and cyanosis becomes manifest. The ankles and legs show oedema, the liver is passively congested and can be felt below the costal arch, tender upon pressure, or causing, even when no pressure is made, epigastric and hypochondriac sense of weight or even pain. Gastro-intestinal disturbances are more marked and ascites may develop. The kidneys show the result of lowered blood-pressure and general passive congestion, the urine becoming scantier, of higher specific gravity, and containing more albumin and casts. In a word, the picture is cardiac rather than renal. The heart's action may be irregular and the pulse small. Gallop rhythm is frequently to be noted. Such a complication as cardiac incompetence, it is needless to say, is serious, with its possibilities of general passive congestion, hydrothorax, extreme ascites, thrombosis, or complete failure of the heart. And the danger from severe uremic manifestations is increased, as the already diseased kidneys are now seriously congested and renal insufficiency is more marked.

Another complication, besides congestion, that may be engrafted on a chronic nephritis is an acute exacerbation of the inflammatory process. Sometimes a cause for such exacerbation can be discovered in an exposure to cold or damp, overexertion, an acute infection like pneumonia, acute bronchitis, or an angina, but often no explanatory cause can be assigned. The urine becomes scantier and of higher specific gravity, the albumin is increased in amount, and casts are abundant; blood may be present. Oedema of the eyelids, face, scrotum, or sacral region may appear. And, as in an acute nephritis, there may be anorexia, nausea, headache,



dizziness, etc. Such exacerbations are not uncommon, and easily pass for acute nephritis unless the previous existence of the underlying chronic trouble is known. Such acute exacerbations may recur from time to time and death is not infrequently due to this cause.

Under certain circumstances hemorrhage is of such a character as perceptibly to modify the course of the nephritis or even seriously to threaten life. Hemorrhage from the kidney may be of this nature. Epistaxis, as already stated, has occasionally proved fatal. The most common serious hemorrhage, however, is *cerebral*. This is usually in or near the internal capsule, is like the ordinary "stroke of apoplexy," and needs no further word of description. It is well, in giving a probable outlook in a case of this form of kidney disease, especially when blood-pressure is high and peripheral vessels sclerotic, to remember the possibility of the occurrence of this vascular accident.

Catarrhal inflammation of mucous membranes is a very frequent, in fact almost constant, occurrence. At times these inflammations are severe, and the bronchitis, gastritis, or enteritis may be regarded as complicating conditions. These inflammations may be looked upon as in part congestive, as in the bronchi, stomach, or bowel, with a failing heart; in part they are uremic; in part, perhaps, toxic, in the sense that the mucous membrane is trying vicariously to eliminate poisons that should be eliminated through the kidney and is irritated by such poisons; in part microbial, infectious organisms more readily attacking the mucous membranes.

The serous membranes seem peculiarly vulnerable during the course of nephritis. Peritonitis, in the writer's experience, has been extremely rare, although mentioned by nearly all authorities as relatively frequent. Pleuritis and pericarditis are much more common, though some of the cases described as pleurisy and pericarditis are probably instances of hydrothorax or hydropericardium. These infections are frequently mild, perhaps due to not very virulent organisms, and the resulting fever and pain may be slight. In fact, both these complications, particularly the pericarditis, are apt to be insidious and to remain latent, and they are readily overlooked. The signs of pericarditis are notorious for their rapid change in character from day to day. Tirard thinks renal pericarditis shows this peculiarity to an unusual degree.

The lowered vitality of the nephritic makes him particularly liable to infectious diseases. Pneumonia is not infrequent (Stewart, 7 per cent. of cases). The mortality, however, is not so much higher as one might expect, except when the pneumonia—often here a broncho-pneumonia—occurs as a complication in the later stages, when cardiac and renal incompetency have become marked and when death seems not far distant even without the complication. Other infections, such as corynebacterium, angina, septicemia, may also occur.

**Diagnosis.**—Not infrequently there is a disparity between clinical diagnosis and pathological findings. Cabot<sup>1</sup> and Emerson<sup>2</sup> have forcibly emphasized this point, making one feel really skeptical regarding our

<sup>1</sup> *Jour. Am. Med. Assn.*, March 18, 1905.

<sup>2</sup> *Ibid.*, January 6, 1906.

ability to make a correct *intra vitam* diagnosis of nephritis. Some of these errors are due to attempts to make a diagnosis with insufficient anamnesis; some are merely instances of an unwise enthusiasm that induces one to attempt to make a too refined anatomical diagnosis, perhaps an impossibility in the particular case.

Some of these discrepancies are, of course, simply errors or blunders, the result of hasty or incomplete examinations by clinician or pathologist. The fact that the arteriosclerotic kidney is frequently present, although a non-albuminous urine is passed, is often overlooked; or the pathologist classes as chronic nephritis what really should be regarded as an arteriosclerotic, atrophic kidney. Again, a small area in the kidney, perhaps a small infarcted patch, may be causing a slight albuminuria and cylindruria and lead to the clinical diagnosis of nephritis, overlooked post-mortem, and the kidney passed as normal. Albuminuria from a congested kidney, from an altered blood-state, or from febrile conditions, may lead to a mistaken diagnosis of nephritis. Carelessness may also lead to misinterpretation of albuminuria due to pus or blood in the urine from some cause other than nephritis. Chronic prostatitis must be kept in mind in connection with this.

Painstaking care in examination of patients particularly with reference to cardiovascular conditions and careful study not of single but of many samples of urine will reduce materially the number of overlooked cases. Furthermore, it is often of far greater importance to decide whether the kidney is functionally normal than to be able to make a diagnosis that is anatomically correct. When after thorough study of a case it is found post-mortem that there is an unsuspected nephritis, one has simply to admit the shortcomings of our means of diagnosis. Non-albuminuric nephritis may be more common than has been taught.

With failing heart, the differentiation from primary *valvular, myocardial, or pericardial disease* (adhesive mediastinopericarditis) is not always easy, and at times is possible only when one obtains knowledge of the previous history. The coexistence of aortic or of stenotic mitral lesions with a mitral leak is evidence in favor of organic valvular disease, as are signs of adherent pericardium. No test is, perhaps, of as much value as the therapeutic one of putting the patient at rest, restricting the diet, and administering suitable remedies, such as digitalis, cathartics, etc. If under these circumstances the heart diminishes in size, the apical murmur becomes louder, and the sound of the pulmonic closure grows sharper and more accentuated; and if with these evidences of improvement in cardiac tone the cedema disappears, the urine increases in quantity, the albumin and casts vanish, one may be reasonably certain that primary nephritis is not the cause of the cardiac incompetency. If, on the contrary, with improvement in the cardiac condition and disappearance of dropsy the mitral murmur disappears or grows fainter, if the aortic closure takes on a sharp, ringing, accentuated character, and if the urine increases to more than the normal with a low specific gravity, and if casts and albumin are constant, one may conclude that there is primary nephritis with secondary cardiac trouble.

The urine of pure *congestion of the kidney* is apt to be more reduced

in amount, of higher specific gravity, and to contain a smaller amount of albumin and fewer casts than when the congestion is superimposed upon a previously existing chronic interstitial nephritis by the failure of the myocardium. Even when congestion is added to the chronic interstitial nephritis, the amount of urine may remain normal and the specific gravity will often be below 1020 or 1018. With the pure congestion from primary heart disease, the amount of urine is often as low as 400 to 800 cc., and the specific gravity is usually 1020 to 1030. The absence of albuminuric retinitis and of typical uremic manifestations may have some weight in influencing one toward the diagnosis of primary cardiac disease.

The difficulty of diagnosis is also great in many instances of *general arteriosclerosis* with enlarged heart and perhaps a systolic murmur at the apex and base from roughened mitral and aortic valves, and with albumin and casts in the urine. Differentiation between the primary nephritis with secondary arteriosclerotic vascular and cardiac changes may not be possible, and in a sense is not always of great practical importance.

If the facts of the earlier history are obtainable, it may be shown that the thickened vessels and enlarged heart were present at a time when polyuria and albuminuria were slight and inconstant, and that they were marked long before any uremic symptoms were manifest. Albuminuric retinitis will be rare, although unilateral retinal hemorrhages may occur. Angina pectoris, irregular action of the heart, and evidences of myocardial degeneration, are more apt to be prominent symptoms than urinary changes or uremic manifestations.

There is seldom cause for confusion of typical cases of either acute or chronic *parenchymatous nephritis* with the chronic interstitial variety. The frequent occurrence of general œdema, the scantiness of the urine, its higher specific gravity, the abundance of albumin, the numerous casts and the blood, stand in striking contrast to the insidious onset, absence of œdema, large amount of pale urine of low specific gravity, with but few casts and but a small amount of albumin. In both the parenchymatous forms cardiovascular changes are less marked and albuminuric retinitis is less likely to be present.

It is not, however, an easy matter to determine in a given case whether there may not be a combination of chronic interstitial nephritis and the acute form, *i. e.*, an acute process engrafted on the chronic, a so-called *acute exacerbation* of the chronic. This condition is by no means infrequent. The urine in many respects will resemble that of acute nephritis; albumin and casts will be plentiful; blood may be present and the amount of urine may be less than normal. Œdema may develop. The existence of a long-standing nephritis may perhaps be suspected from the history of polyuria, thirst, and palpitation; marked enlargement of the left ventricle, sharply accentuated aortic tone, and albuminuric retinitis also point in the same direction. Often, too, a low specific gravity, say 1013, although the other urinary findings are those of acute nephritis, will raise the question of the existence of a long-standing chronic nephritis. Rest and time may clear up the diagnosis as the acuter process disappears, leaving the case a plain one of chronic interstitial nephritis.



It has been stated on a preceding page that in many cases the only diagnosis that is justified by clinical and anatomical facts is the diagnosis of chronic nephritis or *chronic diffuse nephritis*. Such a diagnosis seems to be warranted when in a chronic nephritic we have the œdema, the abundant albumin and casts of chronic parenchymatous nephritis, with the cardiovascular changes, the retinitis, the uremia, and some of the urinary findings of the chronic interstitial variety.

*Secondary contracted kidney* may be recognized if one has had the opportunity of watching the patient go through the stage of œdema and abundant albumin, and has seen the enlarged heart and polyuria appear, with a coincident disappearance of œdema and a lessening in the amount of albumin and the number of casts. Without such a preceding history the best one can do is to consider the case as one of chronic nephritis, differing from the typical contracted kidney only in its tendency to have a larger percentage of albumin than normal, the amount of urine being not as great as in chronic interstitial nephritis and the casts more abundant and darker (Bartels). Some œdema may still be present.

Pure *amyloid kidney* may be recognized by the existence of some operating cause, such as tuberculosis—particularly chronic excavating pulmonary tuberculosis when associated with tuberculosis of the intestine—chronic suppurative processes, or syphilis in its later stages. The anemia and cachexia of amyloid, the dropsy, the enlarged hard liver and spleen, and the frequent diarrhœa from amyloid of the intestine, lend color to this diagnosis. The urine is apt to vary from day to day, both in amount and in its content of albumin and casts. In general it is increased in amount, its specific gravity low, and the amount of albumin considerable. Serum-globulin is present in larger proportion than in ordinary nephritis (Senator). Cardiac hypertrophy, albuminuric retinitis, and uremia are not associated with pure amyloid kidney. In some instances postmortem examination has shown amyloid degeneration in the kidney where a chronic nephritis is also present and where during life there has been no thought of amyloid unless the existence of tuberculosis, syphilis, or suppuration, or an enlarged spleen or liver has aroused suspicion of possible visceral amyloid change.

The stage of *convalescence* from an acute nephritis may prove quite confusing. Here the urine is often increased in amount, of low specific gravity, and the previously large amount of albumin is represented by a small amount or a mere trace that may persist for many weeks, as may also a mild cylindruria. The preceding history is, when obtainable, of great assistance in the diagnosis. The absence of high blood-pressure and of enlarged left ventricle, and the tendency for all the urinary abnormalities to disappear speaks for the absence of the chronic process.

The so-called *physiological albuminuria* may be mistaken for chronic interstitial nephritis, largely because of the absence of œdema and the fact that the amount of albumin is usually slight and inconstant. The absence of cardiovascular changes, the rarity of casts, the fact that polyuria is not noted, should arouse suspicion when this condition is found in the young, that the albuminuria may not be due to an incipient chronic process. Plenty of time must be taken in a thorough study of

such a case to determine as to the periodicity of the albuminuria and the influence upon it of diet, position, and exercise. The writer agrees with Krehl when he states his belief in the existence of a physiological albuminuria—using the poorly applied term physiological to mean that there is no known anatomical, at least inflammatory, change in the kidney—and that complete *restitutio ad integrum* occurs. The amount of albumin in these cases may be considerable. Senator's caution is wise and safe when he advises one to view every supposed case of physiological albuminuria as a possible beginning chronic nephritis, and to regard an albuminuria as physiological only when it is transitory, when the amount of albumin is small, present in one who has not reached adult life, and when it appears only after what may be regarded as a physiologically exciting cause, such as a heavy meal, overexertion, etc.

Albumin due to the presence of *blood* or *pus* in the urine ought not ordinarily to mislead one to a diagnosis of nephritis. The chemical and microscopic proof of the presence of these pathological substances, the direct variation in the amount of albumin with the variation in the amount of blood or pus, the fact that filtering them out removes all or the greater part of the albumin, the absence of casts and of cardiovascular changes and uremia, together with the presence of some cause for the hematuria or pyuria, as stone or tuberculosis in the kidney or bladder, pyelitis, cystitis, prostatitis, etc., would induce one to recognize the albuminuria as the so-called spurious rather than true and nephritic. But combinations of the two conditions may be met with, as when a nephritic is a sufferer from calculous or tuberculous pyelitis; or the case may be one of ascending pyelonephritis, the so-called consecutive nephritis. Under these circumstances filtration and removal of the pus does not by any means remove the albumin; casts are found, and the blood pressure, the retinal findings, and uremic manifestations may give evidence of the existence of a true nephritis.

The thirst, polyuria, and emaciation of contracted kidney may lead one to suspect *diabetes mellitus*. The examination for sugar, with negative result, and the finding of albumin and casts make the diagnosis plain. A low specific gravity, however, should not lead one too promptly to exclude diabetes, for when a diabetic has been drinking large amounts of water the specific gravity of the urine, although sugar-containing, may be below normal.<sup>1</sup> Again, chronic interstitial nephritis may develop during the course of diabetes. When this takes place, not only are there cardiovascular evidences of this occurrence, albuminuria and cylindruria, but the specific gravity of the urine is lowered, perhaps even below the normal, and, strange to say, the glycosuria may disappear. This possible combination of diabetes and nephritis ought not to be forgotten, nor should the fact be overlooked that in some cases of diabetes there may be spells of freedom from glycosuria. A similar caution ought to be given concerning the misinterpretation of urinary findings during diabetic coma. Sugar is occasionally absent during such coma and is scanty. A small amount of albumin is common, and hyaline casts may

<sup>1</sup> Cf. Herrick, *Amer. Jour. Med. Sci.*, 1900, exx

be present in enormous numbers (Külz's phenomenon). Under these circumstances, were one to rely upon the presence of albumin and casts alone, the coma might easily be regarded as uremic and the diabetic features entirely overlooked.

A study of the urine for a short time, with the continued absence of albumin and casts, the unusually low specific gravity, *e. g.*, 1004, and the absence of cardiac, vascular, retinal, and uremic changes, enable one to recognize *diabetes insipidus*. Rarely the two are combined.

The frequent urination of the man past middle years, particularly the frequent nocturnal urination, may be looked upon as due to an *enlarged prostate*, unless the examination of the prostate gland and of the urine be made. Enlarged prostate may, of course, coexist with the nephritis. A trace of albumin or of nucleo-albumin from an accompanying cystitis may add some confusion to the differentiation.

*Cystic kidneys* may cause albumin and high blood-pressure. A careful physical examination will enable one nearly always to feel the enlarged, perhaps roughened, kidneys. Rarely the enlarged cystic kidney is unilateral. Developmental faults, as hypospadias or harelip, are sometimes found at the same time.

There are, of course, numerous errors that are possible when due thoroughness is not exercised in the matter of subjective and objective examination, the mistakes being made chiefly because striking uremic symptoms are looked upon as manifestations of independent diseases, or as due to some other cause than the underlying nephritis, which is overlooked. Such mistakes are fortunately easily avoidable, the study of the urine and of the heart being usually all that is necessary to lead to the discovery of the renal mischief. Without going into details, it may be well briefly to mention a few of these possible sources of error. Among the commoner ones is to mistake as simple *gastritis* or dyspepsia the anorexia, distress from gas, nausea, fulness after eating, epigastric pain, vomiting, or perhaps diarrhoea that are evidences of uremic intoxication.

*Neuralgias* of various types, muscular cramps, or pruritus may have their real nephritic significance overlooked unless care is exercised. And a mistake that seems to be altogether too common is to misinterpret entirely the dyspnoeic, bronchitic, and "*asthmatic*" phenomena; the nocturnal seizures of dyspnoea are very characteristic, and should always lead to a urinalysis. It has been noted that chronic nephritis may resemble *tumor of the brain*, because of the severe headache, vomiting, papillitis, and such cerebral symptoms as dizziness, tinnitus, disturbances of vision, and possibly even delirium or monoplegia. The urinary and cardiovascular phenomena will put one on the right track. The simulation of *malignant disease* is not very close, yet the anemia, emaciation, local gastric disturbances, or perhaps hematuria or melena, may lend still further color to this thought. And without the careful examination so often referred to, it is an easy matter to regard the often vague symptoms of easy tire, nervousness, anxiety, sleeplessness, poor appetite, headache, dizziness, etc., as but evidences of physical or mental overwork, or of "nervousness," or *neurasthenia*. The temporary improvement under



tonics, a vacation, or a short trip away from home may be looked upon as a proof of the correctness of this view. The routine examination of the urine would avoid many a blunder.

The differential diagnosis between uremic *coma*, on the one hand, and the coma of alcohol, opium, diabetes, and such cerebral condition as hemorrhage, embolism, or thrombosis, fracture of the base, meningitis, abscess, etc., on the other, might be discussed at length, but seems unnecessary, as each case has to be studied on its own merits, and no rules or tabular scheme of differential diagnosis will be found to be available as an easy or ready-reference scheme of diagnosis. The facts of the previous history, when obtainable, are often of extreme value. The urine, obtained by catheter if necessary, the high blood-pressure, enlarged left ventricle, the tortuous vessels, the slight œdema, the urinous odor to the breath, and the albuminuric retinitis are all of immense help. The fact that transitory albuminuria may be present after cerebral hemorrhage, epileptic seizures, etc., should not be forgotten. And when fever and delirium occur with uremia the resemblance to the delirium or to the stupor and coma of typhoid or of sepsis may be striking. These cases are not so very infrequent. The writer once saw one of the best clinicians of Europe trip up on the differentiation between purulent meningitis and uremia. Often the diagnosis of uremic coma is to be made by exclusion. It is a pretty good rule to diagnose uremia as the cause of coma only after one has been able to exclude other causes. Possible combinations, such as alcoholism or cerebral hemorrhage with uremia, must not be forgotten.

The toxic condition due to *simple anuria*, when there is suppression of urine, as from obstruction due to a calculus, or following anesthesia, presents some differences from that toxemia due to true uremia, *i. e.*, nephritis. The fact of such difference has been emphasized especially by Ascoli,<sup>1</sup> and seems to be at times clearly made out. There is commonly less headache, less pain, less intractable vomiting, but rather a gradually increasing restlessness, anxiety, sleeplessness, and general weakness. The pulse grows weaker. There is early tendency to stupor, and little delirium, except toward the last, when the slight mental wandering finally merges into a condition of unconsciousness.

**Prognosis.**—Chronic interstitial nephritis is to be regarded as an incurable disease. Recovery is certainly a rare occurrence. Hospital statistics show a frightful mortality from chronic Bright's disease, and the cases there seen by physicians or in the clinics by students, are in serious condition, and many of them clearly but a short remove from death. To get a right view of this matter of prognosis the physician must go back to his statistics of the office consultation room, and his experience in private practice, and not let the college clinic or the ward of the charity hospital appear too prominently in the foreground. When this is done he will be surprised to find how chronic interstitial nephritis is not necessarily inconsistent with years of comfort, happiness, and usefulness, or even with ripe old age. And he learns that while it is

<sup>1</sup> *Die Uraemie.*

wrong to promise a cure to the individual in whom we find early the urinary and cardiac signs of that disease, it is just as wrong to hold out to him the gloomy prospect of a complete invalidism and an early demise.

The patient is entitled to know that the progress may in the natural course of events be slow, that he is fortunate in having had detected in the urine this evidence of weakness on the part of the kidney, that it may be his salvation in leading him to regulate more carefully his habits of eating, drinking, and working, and result in a decided prolongation of life. We must make him realize that a kidney, although hopelessly anatomically diseased, may be functionally healthy and for a long time able to perform its duty.

There is no set of rules that can be formulated by which one may decide as to the prognosis in a given case. One's experience and judgment here play important rôles. The case must be considered as a whole, and attention not fixed too particularly on the amount of albumin, the number of casts, the size of the heart, the condition of the retina, etc. One must, in other words, individualize in the matter of prognosis.

Upon cardiac integrity depends to a great extent the length of time the patient can hope to live. Excessive cardiac enlargement with high blood-pressure and symptoms, such as palpitation, dyspnœa, etc., lead one to fear that cardiac incompetence is imminent. Although rest and treatment may for a time restore cardiac tone and bring about great improvement in the general condition, the rule is that such a breakdown is a sign that the patient is constantly near the danger line, and that degenerative changes in the heart muscle are advanced. Intercurrent affections and acute exacerbations add to the gravity.

The so-called uremic phenomena, when they are pronounced and persistent and when not evidently due to some acutely or temporarily acting cause, are of grave import. Such things as persistent headache, nausea and vomiting, loss of weight and strength, and the development of the cachectic appearance and signs of malnutrition are of this character. A typically "urinous" odor to the breath always seems to be associated with the severer and advanced forms of the disease. Personal experience with albuminuric retinitis tallies with the traditional fact that such a finding is indicative of an advanced kidney disease, and that death is seldom delayed more than two years. The urinary findings are rather uncertain so far as prognosis is concerned. Relative anuria is often of bad import, although it usually depends upon the condition of the heart. Toward the end albumin is apt to increase in amount. Cryoscopy of the urine unless combined with cryoscopy of the blood gives little help in the way of prognosis. Death in the near future is the usual result when convulsions or coma occur.

The outlook in cases of the arteriosclerotic kidney is often grave, because of the attendant coronary sclerosis and myocardial degeneration. Yet many patients of fifty or sixty lead lives of considerable activity, although their vessels and heart show evidence of moderate sclerosis and although the trace of albumin and the few casts show that a similar condition obtains in the vessels of the kidney.

*High blood-pressure*, even to 200 mm., is not necessarily indicative of immediately impending danger. Patients may carry such a pressure for years and enjoy a fair degree of health.<sup>1</sup> Of greater significance in many cases is change in blood-pressure. A pressure that is seen to be going steadily up from month to month, in spite of care on the part of the patient and the exercise of his best skill on the part of the physician, is naturally a cause for alarm, while one that is stationary or that under treatment is lowered to near the normal may make one feel more hopeful as to the immediate outlook. Much may be learned also by watching the blood-pressure during a period of cardiac incompetence.

The outlook in a given case often depends much on the intelligence of the patient and his willingness and ability, both mental and financial, to coöperate with the physician in carrying out treatment.

The way in which death will come in a given case can seldom be predicted. Sudden coma will occasionally overwhelm one who seems to be doing nicely. Or one whose subjective symptoms are slight, whose blood-pressure does not seem dangerously high, succumbs to cerebral hemorrhage. Intercurrent disease, as pneumonia, carries off a considerable proportion. A cardiac death with its dyspnoea and dropsy is reserved for a large number, while many die with uremic intoxication. Oftenest, perhaps, the final scene is a mixture of the uremic and cardiac, a most distressing picture, the only consolation for which is that death when it comes seems a relief from almost intolerable suffering.

**Treatment.**—Not much is actually accomplished, at least consciously, in the way of warding off chronic intestinal nephritis, because little opportunity is offered for explicitly advising as to *prophylactic measures* to be carried out for the purpose of guarding against this disease, for one is uncertain as to who is "threatened" with it. Yet a timely word as to proper modes of living may be of help in this respect in the case of individuals in whose families there is a tendency to chronic Bright's disease and early arteriosclerosis. Warning may be given the worker in lead, the gouty individual, the alcoholic, and the one who is keeping pace with his more vigorous comrades in the strenuous life. Changes in habits of living in instances of this sort will undoubtedly do good in warding off this disease.

Proper treatment of an acute infection, such as scarlet fever, with special watchfulness during convalescence, may prevent the development of acute nephritis that might possibly be the forerunner of the chronic form. Attacks of acute nephritis from whatever cause, and instances of sharp febrile albuminuria, should lead to watchfulness in the future, as they possibly indicate a special vulnerability on the part of the kidney. One should not neglect conditions that may cause chronic intoxications, such as repeated attacks of infectious troubles, malarial fever, oft-recurring tonsillitis, nasopharyngitis, chronic suppurative otitis, chronic bronchitis, syphilis; and one should also, for the same reason, strive to relieve chronic gastro-intestinal disorders. Cystitis and pyelitis should, of course, be relieved when possible.

<sup>1</sup> Cf. Theodore Janeway, *Trans. Assoc. Am. Phys.*, 1913, xxviii, 333.



Prophylactic treatment, however, consists largely not in warding off the disease but in guarding against its more rapid progress. Great good comes from proper advice, properly followed, in the case of the one in whom, perhaps accidentally, the evidences of incipient nephritis are found in shape of a slightly increased blood-pressure, a beginning thickening of the vessel wall, a trace of albumin, or a few casts in the urine. As Osler has somewhat paradoxically but happily said, the man of middle years whose trace of albumin is discovered is to be congratulated, for from this time on, if he be wise, he will be more careful and heed the warning, modifying his excesses in eating, drinking, and working.

The *active treatment* necessarily implies the removal of the operating cause whenever possible. While this cannot always be discovered, and may not always be removable, something may at times be accomplished in the way of checking the progress of the disease by correcting disorders such as those just mentioned. Workers in lead may be instructed as to how to live, still keeping at their work, or, as is usually necessary, advised to give up this, for them, dangerous occupation. The gouty man is given instructions as to diet, the alcoholic warned of the harmful results of pursuing his habits of drinking. The man of extreme business activity is cautioned against a continuance of his excesses in this line.

All these directions are, it will be noted, along the line of preventing a continuance of the previously operating baneful influences, and to this end of sparing the kidney unnecessary work our efforts should from now on be directed. In other words, the damaged organ must be given *rest*.

**Diet.**—A dietary has to be planned that, while not harmful to the kidneys, is palatable and nourishing and will be tolerated for months or years. *Milk diet* alone is here an impossibility. To give enough milk to maintain the strength of an adult who is up and about means the taking daily of several quarts, and this is not always wise, because it adds to the volume of the blood and thus throws extra work on the heart; and besides, it increases the demand made on the kidney in the way of eliminating water, *i. e.*, it violates one of the rules of rest. The protein content of this large amount of milk is also more than is desirable. The taking of such large amounts of milk to the practical exclusion of other foods soon leads to loss of appetite and to various disturbances of the stomach and bowels, with consequent anemia and emaciation. One feels like emphasizing strongly the harm done by limiting the food to milk alone.

The protest here is against the diet being restricted to milk alone. Against milk as an article of food suitable for chronic nephritis nothing can be said. It is nourishing, as harmless in the way of irritating the kidney as any other food, and it supplies a needed amount of liquid. It may with distinct advantage be given to such a patient, and may even be the main article of food for long periods of time.

Closely connected with the question as to the amount of milk to be given is the question as to what amount of *liquid* should be allowed the nephritic. In contracted kidney the necessity for washing out the tubules and freeing them from large amounts of debris does not exist, nor is there, as a rule, a demonstrably great failure of elimination of

solids. The total solids for twenty-four hours often reach the normal. The necessity, therefore, for the huge amounts of fluids sometimes given these patients is not so clear as one might suppose, and a certain contra-indication seems to exist, from the fact that these large amounts demand extra work on the part of kidney, heart, and vessels, organs that one wishes to spare so far as possible.

The limitation of liquids to one and one-half liters per day, as is advocated by some, is perhaps wise, although too arbitrary. This is certainly not enough for many individuals. It seems better to allow some latitude in this respect, to say that one and a half to two liters per day is a fairly average amount, but that a patient's own thirst may be a reasonably safe guide unless it lead to extremes, *e. g.*, one to two gallons per day. Some patients need explicit directions as to the amount of water to be taken; but no hard and fast rule can be given that is applicable to all. It is a good plan for all patients who are taking only a fair amount of liquid, or an amount that is for them a restricted amount, to take occasionally larger amounts, say two to four quarts per day. This plan is pursued by many who make trips several times a year to watering places. The same plan can be carried out at home by having one day a week for a "flushing-out day," a plan advocated by von Noorden.

This limitation of the amount of fluids has been repeatedly advised by von Noorden and his pupils, and is supported by Pel, Koranyi, and many others. Some, however, like H. Strauss,<sup>1</sup> take issue with von Noorden and advise against the too great reduction of fluids, believing that the elimination of toxins and the dilution of the blood outweigh any supposed danger.

*Alcohol* is to be avoided as an irritant of the kidney. Occasionally a small amount of wine with meals may be allowed as a stimulant to the appetite and an aid to digestion, but the physician who permits this should know his patient well and be assured that there will be no excessive indulgence. Tea and coffee need not be interdicted. An excessive amount, however, may not only injure the kidney directly, but may have a harmful influence on the heart, vessels, and blood-pressure. These beverages must, therefore, be taken in moderation. The same statements may be made concerning *tobacco*, the excessive use of which is to be avoided.

Rules as to *diet*<sup>2</sup> in this disease must be general and quite flexible. Temperance and moderation as to food are to be enjoined. An excessive amount of food throws extra eliminative work on the kidney, tends to plethora and obesity, thus making unusual demands on the heart, and

<sup>1</sup> *Berl. klin. Woch.*, May 25, 1908.

<sup>2</sup> Fuller details regarding diet in nephritis, and especially the question of meat as an article of food in this disease, may be found in the excellent discussion of the topic by Leube, in vol. vii of Penzoldt and Stintzing's *Handbuch der Therapie*; in the discussions by Senator, Ziemssen, and others in the *Verhandl. des IX Kongresses f. innere Medizin in Wien*, 1890, and in papers and discussions by Lépine, Grainger Stewart, and others before the International Medical Congress, Berlin, 1900. Diet was discussed in the *London Lancet*, in 1893, by several English writers, among others by Hale White, Ralfe, and Donkin. Much interesting clinical experience is found in a symposium on the treatment of Chronic Bright's Disease published in the *British Medical Journal*, October 8, 1900.

adds to the danger of disturbing digestion. Simple, easily digested foods should be the rule, and these should be taken with regularity, in reasonable amount, and without hurry. Rich and highly seasoned foods should be avoided. There should be but little used in the way of stimulating condiments, hot relishes, sauces, pepper, and other spices, mustard, radishes, cress, rich or strong cheese. Cakes, puddings, pies, pastry, and candies should be eaten sparingly, as disorder of the stomach and bowel is liable to follow their too free use.

The chronic nephritic cannot, without harm, be too long deprived of *protein*. The amount estimated as necessary, about 80 to 90 grams, would require the drinking daily of over two liters of milk, or the taking of fifteen eggs, or 400 grams of meat. It seems far better to let this amount be taken not in the shape of milk alone, nor of meat or eggs, but, as a mixed diet, some milk, perhaps a liter, and a moderate amount of meat and eggs. Most patients, at least in this country, must be restricted very materially in the amount of meat taken, for, as a rule, they are heavy meat eaters, many taking it freely three times a day. Meat once a day, with an occasional egg, will be found not only not harmful, but really of benefit, helping appetite, increasing the strength, and improving the condition of the blood. This, with the liter of milk and the small amount of protein contained in the other food taken, will furnish the amount of albuminous food necessary to meet the demands of the body, and to make up for the inconsiderable loss of albumin through the urine. Dark meats taken in these moderate amounts are not to be regarded as injurious. Whether meat is advised or not will naturally depend on whether it is well handled by the stomach and bowel. Harm may come from forcing the meat diet when it produces gastro-intestinal disturbances. Houghton<sup>1</sup> believes that when in the course of a nephritis characterized by high blood-pressure there is indican in the urine, treatment designed to lessen the amount of protein putrefaction in the bowel will have a tendency to lower the blood-pressure by preventing the absorption of substances which accumulate by reason of the reduced kidney capacity. Temporary removal of meat and eggs from the dietary will here be indicated.

Soups that are rich in meat extractives, such as contain an abundance of "stock," should be taken in moderate amounts only. Gruels and simpler soups may be taken more freely. Raw eggs are probably more harmful than cooked eggs, although Leube<sup>2</sup> justly observes that there are few people who prefer raw eggs, and believes that the danger from taking a few uncooked eggs daily is not so very great.

To make up the caloric value necessary for an adult, considerable *carbohydrate and fat* must be taken in addition to the protein. Of the latter enough is commonly ingested in the form of butter, cream, oil, and as a constituent of some of the other foods. The carbohydrate (300 to 400 grams) is supplied by cereals of various kinds, bread, vegetables, especially the young and green vegetables, and fruit. No special

<sup>1</sup> *American Medicine*, October 7, 1905.

<sup>2</sup> Senator, *Berl. klin. Woch.*, 1882, No. 49; Csáthy, *Deutsch. Archiv f. klin. Med.*, 1891, xlvii, 179; Ott, *ibid.*, 1894, liii, 608.



limitations need be placed as to kind or amount of these foods. Asparagus is regarded by some as harmful, although it may probably be taken without injury, if not used to excess.

The dietetic treatment may be summed up in a few words by saying that the diet must be a mixed diet from which all highly seasoned, spiced foods and alcohol are excluded; meat and other proteins are to be taken in moderate or small amounts; cereals, vegetables, and fruits freely; the sweets sparingly. Milk is allowed freely, but neither it nor water is to be taken in excess. The total amount of food taken should not be excessive; the nephritic should not be a "heavy eater."

*Physical overexertion* is contra-indicated; not only does this act injuriously on the heart, that must be spared all unnecessary strain, but it makes a call upon the kidney to carry off an added amount of debris, the result of this excessive muscular exertion. Similarly, mental and nervous overwork may have to be curtailed. The keynote to the treatment in these respects, as in the matter of diet, is moderation. The patient with nephritis must have impressed upon him the fact that although he may be temperate as regards the use of alcohol, he may by intemperance in other respects, food, work, worry, etc., be doing himself as much harm as though he were indulging in alcohol to excess. Absolute rest in bed is seldom necessary for the patient with chronic interstitial nephritis, except during periods of acute exacerbation, cardiac failure, or in the later stages of the disease, unless it be, perhaps, when the patient first comes under the care of the physician, who may then deem it wise, in order to "get a line" on his patient, to put him to bed for a few days of careful observation. Physicians at times prescribe too much abstention from muscular exercise. The nephritic needs such exercise. Carefully regulated walking or gymnastics, or in selected cases massage, may be of benefit. Even mild and systematic mountain climbing may not be contra-indicated. It is surprising how, at times, a patient who has been confined to the bed or to the house will, on being allowed moderate exercise in the open air, show improvement in muscular strength, heart tone, blood condition, appetite, and show no harmful effects in the work of the kidney as evidenced by the urine.

But relative rest, as above described, is of great importance. Business men must be encouraged to throw off some of their burdens upon younger shoulders, and instead of putting new irons into the fire, to take out a few. The yearly vacation should be lengthened, and, when possible, frequent trips away from business cares should be taken, in which the main occupation should be idling, with mild exercise in the way of walking, golf, fishing, etc., rather than severer sport.

This naturally leads one to consider the value of special *climates* and of watering places. The main value of the life at such watering places lies in the change from the former routine work of the patient, the rest and relaxation in which he indulges, and his greater care as to diet. The use of the waters, too, inducing free catharsis and diuresis, is, unless long continued or too freely employed, of advantage, giving the patient the benefit of the "flushing-out" period, to which reference has been made. There is for this disease but little special virtue in any particular

water. In general, the alkaline waters, or, with anemia, the chalybeate waters, are to be preferred. Much of the advantage that comes from the water cure is dependent on the local conditions that prevail and upon the climate. Unless the patient is to have a reasonable degree of comfort, at least approaching that of his own home, he might better let well enough alone and not leave his pleasant bed and board. Occasionally a plain, unvarnished talk with the patient regarding the water cure is advisable, for he may have the notion that is quite prevalent that if he can only go to this or that spring he will be at once greatly benefited or cured, and he is willing to make sacrifice of time, money, and comfort. It is due him to know, and a kindness is done by informing him, that a cure is not to be looked for, and that more is to be thought of in his going to the springs than the water alone; one must look into the matter of climate, surrounding country, food, sleeping accommodations, companions to be met at the resort, possible amusement, etc.

It is often better to disregard entirely the supposed water-cure feature and to have the patient go to some pleasant place or resort for an outing and a period of rest. In winter a dry, warm climate is desirable, such as that of southern Texas, New Mexico, Arizona, California, Mexico, Egypt, southern Tyrol, or the Riviera. In summer a cooler locality should be selected, and Canada, Northern Michigan or Wisconsin, the mountain regions of New England, New York, Virginia, or Colorado, may be sought, where there is the attraction of beautiful scenery and the advantage of pure air without too much heat. In the mountain regions mountain climbing must be interdicted. He must be advised to guard against sudden changes in temperature and unnecessary exposure to cold. Woollen underclothing or handy outer garments are great helps in this direction. Cold *baths* are to be avoided and the home physician must caution his patient, before he goes away, against the too free use of baths often advised because of some supposed curative effect. The chronic nephritic, with his heart perhaps on the verge of breaking down, is one who must exercise considerable care in the way of taking baths which are too prolonged or too hot.

To the physician having in charge a patient with chronic interstitial nephritis there is no problem presented that is more important, yet at the same time more perplexing and difficult of solution in the individual case than that of how rightly to treat the *heart*. Cardiac hypertrophy and vascular hypertension are salutary conditions, compensating in a measure for the renal lesion; blood-pressure must not, therefore, be allowed to become too low. On the other hand, extreme hypertrophy and excessively high blood-pressure carry with them not only some unpleasant subjective symptoms, such as headache and dizziness, but constantly threaten such serious accidents as cerebral hemorrhage or cardiac incompetence and dilatation. How to steer the safe middle course between these two threatening conditions is indeed a perplexing question.

When the heart has given out and dyspnoea, cyanosis, oedema, and the other well-known symptoms and physical signs of incompetency are present, the general object of treatment is clearly to relieve the work of the overburdened heart as much as possible, and to use means to

increase its efficiency. These patients should be put to bed for several days or weeks. The diet should be greatly reduced in bulk, a nourishing, concentrated food being taken, such as eggs, cream, or cereals. The bowels should be freely opened by cathartics. *Digitalis* in doses sufficient to produce a perceptible impression on the heart should be given. No drug is of such value under these conditions as digitalis, and yet no drug requires more judicial skill and trained experience for its proper use and for a correct interpretation of its effects. The tincture in doses of 5 to 15 drops, the infusion freshly prepared from the leaves, 1 to 4 drams (4 to 14 cc.), or the powdered extract,  $\frac{1}{5}$  gr. to  $\frac{1}{3}$  gr. (gm. 0.013 to 0.02), are what the writer most often uses. *Digalen* or *digitalin* may also be employed, particularly when subcutaneous therapy is advisable. The results from the former are sometimes excellent.

As substitutes for digitalis, *strophanthus* may be employed, and as adjuvants, caffeine or strychnine, or when prompt stimulating effects are needed, camphor may be employed hypodermically, from 1 to 3 grains (gm. 0.06 to 0.2) dissolved in 10 to 20 drops of olive oil, being injected perhaps several times a day. Venesection is at times of wonderful benefit under these circumstances; 300 to 500 cc. should ordinarily be removed, and occasionally this should be repeated in a few hours or more; even 500 to 700 cc. may be taken at the first bleeding. Baccelli<sup>1</sup> has advised a somewhat novel method of bleeding, using the dorsal vessel of the foot rather than the veins of the arm, as is common. Ice to the precordia may help check excessive palpitation, and morphine is often of great help, especially with pain, restlessness and sleeplessness. The results from the treatment of cardiac incompetence can seldom be predicted. Often the breakdown of the heart is the beginning of the end. But it is remarkable how many of the patients whose condition seems truly desperate may be pulled together again, and enjoy months or perhaps years of comparatively fair health.

How best to treat the *high blood-pressure* is a more difficult question. When present, the general rules as to diet, exercise and care of the bowels must be scrupulously lived up to. It is remarkable what may sometimes be accomplished in some of these cases by what may be called a temporary starvation plan of treatment, cutting down greatly the bulk of food taken, both solid and liquid, and employing concentrated but not bulky food, and not too much of that. Blood-pressure will sometimes under these circumstances be promptly lowered, and a general improvement in the condition of the patient will follow. Relative rest or perhaps even rest in bed for a time may be important. The bowels should be kept open, although not loose enough to make the patient feel weak. When the pressure is very high and accompanied by severe headache, dizziness, and sleeplessness, bloodletting will often give prompt relief for the time being. One may sometimes see marked improvement in subjective symptoms and quite a drop in blood-pressure follow a spontaneous hemorrhage, such as a nosebleed; and the bleeding under these circumstances may be encouraged rather than checked.

<sup>1</sup> *Il Policlinico*, 1907, xiv, p. 18.



Drugs for the lowering of blood-pressure are rather uncertain in their results, at least so far as lasting results are concerned. Nitroglycerin, gr.  $\frac{1}{100}$  to gr.  $\frac{1}{40}$  (gm. 0.0006 to 0.0015), will, if given often enough, sometimes work wonderfully well. It must be given, however, not in any fixed dose, but in doses large enough to produce results, at times even gr.  $\frac{1}{25}$  (gm. 0.0025) in one who has become habituated to its use. It is too often disappointing, results being nil, or a beating and throbbing headache follow the use of even small doses. The nitrites, *e. g.*, nitrite of sodium, gr. j to v (gm. 0.065 to 0.32), may be given in solution, the physician feeling his way with this remedy as he does with nitroglycerin, and always beginning with a small dose; erythrol tetranitrate is a favorite with some. Potassium iodide in small doses, gr. v (gm. 0.32), may sometimes be given with advantage. In fact it seems at times, when given for prolonged periods—months or years—to exert a very perceptible influence in softening the pulse and lowering blood-pressure, and while one must realize that there is danger of serious effects in the way of iodism from the giving of too large doses in cases of chronic nephritis—the writer has seen a fatal case from such overdosing—one is justified in giving the remedy in these small doses and for a long time. It is, of course, wise to stop occasionally for a few days during this prolonged period, and not to give it without any interruption. The favorable effects that are occasionally seen in some cases—not necessarily the syphilitic ones—seem unquestioned. It has sometimes seemed that good has followed the use of Donovan's solution (liquor arsenii et hydrargyri iodidi) in small doses, one drop three times a day.

There is perhaps a tendency to use the vasodilators too early; although blood-pressure may be high, this is not always an indication for the immediate adoption of measures for its relief; such high pressure may be a compensatory necessity.

The demands upon the kidney should be as light as possible, not only by regulating the kind and amount of food, the amount of physical and mental work, as already specified, but by striving to have the skin, lungs, and bowels do a part of the work of *elimination*. This has already been discussed in speaking of the treatment of parenchymatous nephritis, and need not be repeated here in any detail. Little can be done in the way of assisting elimination through the lungs save to keep up the action of the heart and to see to it that the patient has plenty of fresh air, both day and night. Daily warm or tepid baths should be taken to keep the skin in good condition, and those who have always been accustomed to the cool morning sponge bath will not be harmed by continuing in this way, being careful to avoid too severe or too prolonged chilling of the body, and being sure to secure a reaction. Occasional hot baths may be taken just before retiring. Sweats are not indicated, as a rule, unless uremia is threatening or œdema is marked. When œdema is pronounced in this form of nephritis, it is, as a rule, due either to an exacerbation of the chronic process or to cardiac weakness. Under the latter circumstances sweats are to be used with great caution, for fear of aggravating the condition of the heart. The bowels should be kept open, although free catharsis is seldom necessary, save when severe

uremic conditions are threatening. Ordinarily, by regulating the diet, using plenty of fruit, green vegetables, coarser cereals, etc., the bowels may be made to move daily. When necessary, a morning saline purge may be given; or some of the vegetable laxatives, such as cascara, aloes, or senna, may be given at night. Elaterium, a brisk calomel purge, or large doses of the salines may be helpful when coma or convulsions seem threatening or drastic catharsis is for other reasons indicated. Enemas may be of service in regulating the bowels.

Venesection in the case of uremia may be mentioned as an attempt to secure vicarious elimination when the kidney is failing in its function, as some toxic material is removed in this way.

Elimination through the avenue of the kidney itself, presumably the healthy parts of the kidney, is aimed at throughout the whole course of treatment by regulations as to diet and drink, by keeping up the action of the heart, by the institution of "flushing-out" days, etc. Special efforts, however, are made in this direction by the use of diuretics, when, for any reason the amount of urine or its content in solids is deficient. Digitalis and caffeine, acting largely through the heart, are of great value. Other remedies are the citrate and acetate of potassium and the sodium-theobromin-salicylate (diuretin). This latter remedy ought to be given fresh, before it has been long exposed to the atmosphere, and unaccompanied by any acid which renders it inert. In doses of 60 to 100 grains (gm. 4 to 6) daily it is sometimes an efficient diuretic. Its good effects are most often seen when the relative anuria is largely dependent on cardiac weakness, with resulting renal congestion. Theocin in doses of 3 grains (0.2 gm.) will often produce diuresis. Lemonade containing cream of tartar may also be used as a diuretic drink.

*Uremia* is discussed elsewhere, and only a bare outline of its treatment will be given here. As a matter of fact, much of the treatment already described is in a sense the treatment of uremia. Should uremic coma or convulsions seem to threaten, as shown by severe headache, vomiting, sleeplessness or delirium, dyspnoea, muscular twitching, high blood-pressure, with irritable heart and perhaps gallop rhythm, vigorous measures must be instituted. The patient is kept in bed, the bowels are opened by a colonic flushing, and a brisk purge of salts, calomel, or perhaps elaterium is given. A minimum amount of food is allowed for two or three days. Venesection will often give temporary relief, lessening the toxemia, lowering blood-pressure, and relieving some of the strain on the heart. Venesection may be followed by the use of normal salt solution, given subcutaneously, 500 to 1000 cc. *Lumbar puncture* will sometimes relieve symptoms temporarily.<sup>1</sup> Just how this is brought about is not entirely clear, although the escape of a large amount of cerebrospinal fluid under high pressure serves to show that Traube's notion concerning uremia has at least a color of truth. Digitalis and caffeine may be necessary, or, on the contrary, help may come from nitroglycerin. Morphine is often indispensable. It relieves pain, restlessness, insomnia and delirium, helps to quiet the action of the heart, and at times actually

<sup>1</sup> See Willson, *Jour. Amer. Med. Assoc.*, July 1, 1905.

seems to promote diuresis. Chloralamide is a favorite sedative with many. Convulsions may demand bromide or chloral, although morphine is more reliable and no more harmful. Chloroform is indicated when convulsive seizures are recurring frequently.

*Edema* in chronic interstitial nephritis is not common. When it occurs, it is due either to the weakened condition of the heart, when it would be treated in the manner already outlined, or to an acute exacerbation of the chronic process. Its treatment under this latter circumstance is that described under acute and chronic parenchymatous nephritis.

*Complicating conditions*, or symptoms that become specially aggravated, may need special attention. The anemia is often benefited by iron. Basham's mixture (*mistura ferri et ammoniæ acetatis*) in doses up to  $\mathfrak{z}$ ss (14 cc.), is a non-irritating preparation that acts also as a diuretic. Tincture of the chloride of iron is less easily tolerated by the stomach, but when given in plenty of water after meals may be used in doses of five to thirty drops. Some regard iron, particularly in this form, as having a beneficial effect, not only on the anemia but on the nephritic process itself, a belief that is, however, not very widespread. The iodide of iron or any of the other preparations, such as Blaud's mass, or the scale preparations, may, if preferred, be employed. Anemia is also combated by an abundance of fresh air, moderate exercise, and—a point of great importance—by seeing that in our endeavors to regulate the diet so as to suit it to the nephritic we are not really giving our patient food that qualitatively is improper and quantitatively is poor in caloric value. Relief of gastro-intestinal disturbances also contributes to improve the condition of the blood. Much stress ought to be laid on attention to the blood condition, not alone because when anemia is marked such annoying symptoms as weakness, dizziness, and palpitation become aggravated, but because with impoverished blood the power of the body to resist the disease becomes materially lessened, and the heart will not compensate as it should for deficiencies of the kidney.

Careful attention to diet as specified, with the use of cathartics when necessary, will keep the alimentary tract in fair condition. In the later stages, however, *symptomatic treatment* will be demanded. Bitter tonics, as aids to appetite and digestion, may be indicated. The old-fashioned combination of tincture of *nux vomica* with hydrochloric acid will often serve a useful purpose. At times an acid condition of the stomach will be relieved by a few doses of soda or magnesia, or the mixture of rhubarb and soda. In some instances resorcin will relieve the distress from pressure and gas that follows eating. In extreme cases an abstinence from food for a day or two, with rectal feeding and enemata of salt solution, or the limiting of the diet for several days to the simplest articles, such as milk or rice water, will be necessary. Occasionally lavage gives relief. Hot applications or mustard plasters to the epigastrium may be tried; when nausea, vomiting, and epigastric distress are extreme and unrelieved by dietetic measures, the use of stomachics, and aids to digestion. Bismuth, oxalate of cerium, drop doses of carbolic acid, and various other remedies may be tried to help quiet the rebellious stomach, but they are very unreliable. At times very minute doses of



morphine by the stomach may be of service, or, what is better in the bad cases, a hypodermic of morphine, giving the patient a quiet sleep and freedom, for a few hours at least, from the persistent retching and vomiting, following which sleep he may be relieved for a time of the severe gastric distress. Diarrhœa is often benefited by giving a sharp purge of castor oil, salts, or calomel, followed by some of the vegetable astringents, such as tincture of kino. Tannigen in 5 grain (0.3 gm.) doses may be of service. Vomiting and diarrhœa may reach a stage where they are practically intractable.

*Headache* is relieved for a time by not overloading the stomach, keeping the bowels open, together with moderate exercise in the open air. But these simpler means will not quiet the suffering in the later stages. Here bromides may be necessary or an occasional dose of one of the coal-tar preparations, *e. g.*, acetanilid, gr. iij (gm. 0.2), with perhaps  $\frac{1}{3}$  or  $\frac{1}{2}$  grain (gm. 0.02 to 0.03) of codein. Care must be taken not to put these coal-tar preparations too freely into the hands of patients, as the habit of using them too often is easily acquired, and the effects are often harmful. At times headache is relieved by lowering blood-pressure by nitrites. The plethoric individual with high blood-pressure may be bled. Later, morphine will have to be resorted to for the relief of the excruciating pain and to give sleep. *Morphine* is naturally a remedy that one should very rarely use in the earlier stages of chronic nephritis, because of its tendency to lessen secretions, and because of the danger of inducing morphinism. It is in the later stages of the disease that the greatest relief is afforded by this drug, which may be employed in the same way and for the same reasons that it is used in the later stages of carcinoma or of pulmonary tuberculosis, *viz.*, to contribute to the comfort of one with an incurable malady. The good that comes from the relief of pain, vomiting, dyspnœa, and sleeplessness more than makes up for any effect on the secretions or possible morphine habit of a few weeks' duration. Bromides, codein, or heroin and other measures may be tried before resorting to morphine.

Other annoying symptoms must be treated according to the principles that govern their treatment under other circumstances. The same is true of complications such as cerebral hemorrhage, pneumonia, or pleurisy. A word of caution is perhaps not out of order regarding the use of drugs that may seem indicated for these complications. Such drugs as salicylates, carbolic acid, or alcohol, must be given with care because of the danger of irritating the already injured kidney. The same may be said of the use of anesthetics; anesthesia in the case of the nephritic should be as brief as possible, for an exacerbation of a chronic nephritis is sometimes due to the use of ether or chloroform.

The treatment of nephritis by supposed *specific* remedies, drugs, sera, or such things as raw kidneys, seems to be wholly without good results.

*Surgery*—the decapsulation of or incision into the kidney—has been advocated as a means of treating nephritis. Some of the most ardent advocates of this procedure believe they are warranted in advising this operation in every case of chronic nephritis as soon as the diagnosis is made, provided the patient is not practically in extremis, and provided

a skilled surgeon is at hand. There follows, Edebohls believes, an "arterial hyperemization of the kidney. The result of this improved circulation in and between the tubules and glomeruli is the regenerative production of new epithelium capable of carrying on the secretory function." As a routine treatment it has not the support of the profession. And when we think of the nature of a chronic interstitial nephritis, for instance, with its local renal fibrosis, its widespread cardiovascular changes, the toxemic origin of the condition, the influence of heredity, etc., it is difficult to understand how the improvement of the mechanical conditions in the kidney or even of its nutritional activity can work a cure. Temporary improvement is all one would expect, and, remembering the natural variability in symptoms in chronic nephritis, in the amount of albumin and casts, and noting, too, it must be added, the loose way in which diagnosis has been made in some of the cases recorded as instances of cure of chronic nephritis, one is forced to ask whether the recovery in some instances may not have been from an acute nephritis or possibly from some non-nephritic albuminuric condition.

In cases of acute nephritis and of congestion in which the kidney is swollen and the capsule tense, Harrison and others have advised a splitting of the capsule or its puncture for the relief of tension. Marked improvement has been seen to follow this procedure, although the well-known spontaneous recovery of most cases of acute nephritis makes one doubtful in a given case as to what benefit has really been derived from this particular treatment.

The conclusions of David Newman<sup>1</sup> represent, perhaps, the views of a surgeon who, while prepared to do a radical operation, is yet conservative. He says: "The conclusions I have come to regarding the efficiency of incision of the capsule or of cleavage of the cortex are: (1) That the operation gives marked relief to the renal pain of chronic Bright's disease. (2) That in cases of hemorrhage, in which the bleeding is practically limited to one side, the operation should be recommended, as it has been frequently followed by cessation of the hemorrhage in chronic Bright's disease. (3) In cases of movable kidney associated with albuminuria, hematuria, tube casts, or blood casts, when due to causes resulting from the displacement, after the operation of incision and fixation these symptoms disappear permanently, but when coincident with Bright's disease only temporary good is effected by operation. (4) Anuria, dropsy, and dyspnoea may be temporarily relieved in chronic Bright's disease, but a cure is not effected. (5) That in anuria, with uremic symptoms arising in the course of acute or subacute infective nephritis, free incision of the capsule and cortex, by relieving the tension and congestion, enables the organ to resume its function, as shown by active secretion of urine from both kidneys after the operation.

In general, it may be said that the profession looks askance, and rightly, at the indiscriminate operation upon every patient who has albumin and casts in the urine, and while in individual cases operation may perhaps be justified, an operation upon every case of nephritis is to be condemned.

<sup>1</sup> *Brit. Med. Jour.*, October 8, 1904, ii.

## AMYLOID DISEASE OF THE KIDNEY

THE name "amyloid" was applied by Virchow to this particular form of degeneration. The name is a misnomer, as the substance is not starchy; it seems to be closely related to if not identical with some of the albuminous bodies. What is the mother substance and in what way amyloid material is deposited in the tissues by the blood are questions that, along with others dealing with the nature and pathogenesis of the amyloid substance, need not be fully discussed in an article dealing chiefly with the clinical aspects of amyloid degeneration as it affects the kidney.<sup>1</sup>

**Etiology.**—Rokitansky's observation (1842) that amyloid degeneration in general was found in connection with a cachectic state induced by chronic suppuration, syphilis, or tuberculosis, has been abundantly confirmed, as also his statement that it was, as a rule, a general process not limited to one organ, but appeared simultaneously in several, such as the liver, spleen, and kidney. Foremost among these etiological factors stands chronic suppuration, such as is seen in unhealed empyema of the chest, chronic osteomyelitis, pyelitis, bronchiectasis, etc. Tuberculosis—particularly chronic tuberculosis of the lung with extensive cavity formation, tuberculosis of the intestine, tuberculosis of bones and joints with fistulous communication with the surface—is another cause, perhaps, as some contend, the commonest one. But it is possible that tuberculosis *per se* has less special influence in the production of amyloid than has the accompanying secondary pyogenic infection, as is the case in phthisical cavities, and bone and joint tuberculosis with fistulæ. Syphilis is a third cause, especially late syphilis, the so-called tertiary form. Malarial cachexia, gout, lead poisoning, leukemia, carcinoma, beriberi, hypertrophic cirrhosis of the liver, actinomycosis of bone, rickets (syphilis?), have been regarded as rare and occasional causal factors. For a few cases no cause has been discovered. The earlier recognition and intelligent treatment of tuberculosis, syphilis, and suppurative affections contribute toward the eradication of amyloid disease. Experimentally, amyloid has been produced by some of the pus germs. This artificial amyloid at times develops with wonderful rapidity.<sup>2</sup> Chronic inflammatory and fibrotic changes in the kidney are not infrequently found associated with amyloid degeneration in this organ. Both conditions may be due to a common cause or the one condition may in some way be the result of the other.

*Age and sex* seem to have little influence except as they predispose to the contributing causes. Males are oftener affected, and the period of young adult and middle life furnishes the greatest number.

<sup>1</sup> In addition to standard text-books on pathology, among many other references that might be given, the following may be consulted on this topic: Rokitansky, *Handbuch der path. Anat.*, 1842, iii, 421; Virchow, *Arch. f. path. Anatomie, etc.*, vi, viii, xi; S. Wilks, *Guy's Hospital Reports*, 1856, ii; Lubarsch, *Virchows Archiv*, 1897, cl; Petrone, *Arch. de Méd. Expér.*, 1898, x; Davidsohn, *Virchows Archiv*, cl; J. Nowak, *Ibid.*, cliii; Neuberger, *Verhandl. der Deutschen patholog. Gesellschaft*, 1904.

<sup>2</sup> Cf. Krawkow, *Centralbl. f. allg. path.*, etc., May 20, 1895, vi.



**Pathology.**—The amyloid kidney is large, firm, and heavy, except when the amyloid degeneration is associated with a chronic indurative fibrosis, under which circumstances the kidney may be small, granular, and to the naked eye resemble the kidney of chronic interstitial nephritis. The kidney is pale, smooth, and the stellate veins stand out distinctly. The capsule strips readily except in case of association with fibrous changes. The section shows a smooth, glistening surface, with clear differentiation between the deep red pyramids and the wide, lighter, waxy-looking cortex. The glomeruli show distinctly, many of them “projecting like glistening dewdrops.” Washed with a solution of iodine in potassic iodide (Lugol’s solution), some of them stain a dark mahogany brown, showing the presence of amyloid material. The same color may be made out in other regions, showing the walls of vessels involved.

It is in the bloodvessels of the kidney—the muscular coat of the arteries especially—that the amyloid change is to be made out. The extent, however, to which the vessels are altered varies considerably. The glomerulus may be converted into a structureless, homogeneous, waxy-like ball. Not only is each affected glomerulus apt to show an irregular patchy distribution of the amyloid changes in the capillary walls but the different glomeruli are very unevenly affected. The microscopic contrast between amyloid and normal tissue is more clearly brought out by staining. The order of frequency with which the different vessels are affected is variously stated, all observers, however, agreeing that the glomerular vessels stand at the head of the list. The afferent arteries, the vasa recta, the efferent vessels, the intertubular capillaries and arteries of the medullary substance, the capillaries of the cortex are in irregular order and, to varying degrees, also attacked. Even Bowman’s capsule and the membrana propria of the tubules may show the change, and at times the epithelial cells themselves, the interstitial tissue and the capsule of the kidney.

The remainder of the kidney is seldom normal. Frequently, and especially when the kidney is macroscopically like the large white kidney, the changes are indistinguishable from those of chronic parenchymatous nephritis. In other kidneys the development of fibrous tissue predominates, and the condition might be classed as chronic diffuse nephritis, or as granular atrophy. The contracted amyloid kidney is believed by some to be met with oftener when syphilis is the primary disease.

Along with the renal changes are to be found the lesions of the primary disease, the suppuration, tuberculosis, or syphilis. There is also an anemia, sometimes pronounced, and oedema is often present. Cardiac hypertrophy and arteriosclerosis are probably never the result of the amyloid disease of the kidney, but they are sometimes found in the cases in which amyloid is combined with chronic nephritis with induration. Lastly, amyloid degeneration of other organs is present. Very rarely the amyloid kidney alone has been found—in from 7 to 10 per cent. of cases.<sup>1</sup> Generally, however, similar changes are found in the

<sup>1</sup> Cf. Rosenstein, *loc. cit.*, p. 393; also *Bull. Nordisk. Medic.*, Band xii, Heft 1.

spleen and liver and not infrequently in the suprarenal gland, the wall of the intestine, or even in the heart.

**Symptoms and Diagnosis.**—Mild cases cannot be recognized. A suspicion that amyloid exists might arise if an efficient cause is present, and if the albuminuria and other urinary findings are not typical of simple nephritis. In more advanced cases the patient is anemic and even cachectic in look. Œdema may be marked, even to the extent of hydrothorax and ascites. Disturbance of the stomach and bowels is often present, a diarrhœa being sometimes the result of the amyloid degeneration of the intestinal wall. The spleen is enlarged, hard, and palpable, as is the liver. The pulse is usually somewhat rapid, and is not of high tension. The heart is not hypertrophied.

The *urine* is usually increased in amount, pale, of low specific gravity, clear, and with but little sediment. The solids are but little altered. It is rich in albumin, and Senator showed that the percentage of globulin was unusually high. Casts, especially hyaline and granular, are present, although not in such large numbers as the amount of albumin would lead one to expect. Blood is rare. Both the amount of urine and of albumin seem to be quite variable, and the specific gravity is sometimes not reduced. Even in the same patient there may be remarkable variations from day to day. Cases of amyloid of the kidney without albuminuria have been described.<sup>1</sup> Leube<sup>2</sup> reports an interesting case of a boy with vertebral tuberculosis and abscess formation, in whose urine no albumin was found, although daily examinations were made for weeks, as renal amyloid was suspected. At the autopsy there was found not only amyloid of the liver and spleen but the microscope showed unmistakable amyloid of the glomeruli and vasa afferentia of the kidney, a condition in which one would expect albuminuria. Rosenstein, Litten, Wagner, and others, report cases without albumin.

There is as much variation in the general appearance of the patient and in the constancy of the other symptoms as in the urine. Instead of the typically weak, pale, cachectic, emaciated individual with the muddy complexion and with the swellings of dropsy, the patient may be fairly strong, of ruddy complexion, fat, and with no dropsy. While the color may, as just stated, exceptionally be fairly good, there is commonly a pallor, even although the musculature and fatty panniculus are well preserved. This is due to the secondary anemia that is present.

Uremia, at least uremia to be recognized as such, is extremely rare. Death is usually from gradual wasting and exhaustion, or due to complicating conditions, such as pneumonia, pleurisy, or peritonitis. Coma, toward the end, is commoner than convulsions; and even when the amount of urine is greatly diminished or nearly suppressed, headaches, uremic dyspnœa, and convulsions are rare, the condition resembling more the toxemia of anuria than that of true uremia. Retinitis is rare.

When, however, the amyloid has been implanted on a kidney, the seat of a chronic interstitial inflammation, the cardiovascular changes, the retinitis, and uremia may be prominent.

<sup>1</sup> Cf. Straus, *Soc. Méd. des Hôpit.*, June 10, 1881.

<sup>2</sup> *Diagnose der inneren Krankheiten.*

It is thus seen that no clean-cut picture of amyloid disease of the kidney can be drawn. The diagnostic features may be summed up much as they are by Leube when he says that amyloid of the kidney is only to be diagnosed when the liver and spleen—or at least one of these two organs, especially the spleen—are enlarged and hard as they are with amyloid degeneration; when at the same time there is a long-standing tuberculosis, suppuration, or syphilis; when the urine, although increased in amount, of low specific gravity, clear, and with but a faint sediment, is yet rich in albumin; and when the cardiovascular changes of chronic interstitial nephritis are lacking.

**Prognosis.**—Virchow<sup>1</sup> declared in 1885 that amyloid was incurable, that healing in the strict sense could not take place. Yet the process seems at times to remain stationary, and it is believed that at least a functional recovery occasionally ensues. This possibility is given some support by the observations of Rachlmann,<sup>2</sup> who saw amyloid of the conjunctiva disappear. Clinically, however, amyloid kidney when far enough advanced to be recognizable is almost invariably fatal. Death may, however, be delayed for many years, even five or ten. Much depends upon the underlying disease, its amenability to treatment, the gravity of the accompanying nephritis, and the condition of the stomach and bowels. Some think the course of amyloid of the kidney due to syphilis is more prolonged than when due to other causes, and that syphilitic amyloid offers a more favorable outlook. Tirard<sup>3</sup> states that the lung symptoms of pulmonary tuberculosis frequently undergo improvement with the development of the renal affection.

**Treatment.**—This consists in the early treatment of the primary disease. The proper handling of this disease may prevent amyloid. Early treatment, even after amyloid has developed, may retard the progress of the renal disease and produce, for a time at least, a functional recovery. Treatment of such conditions as chronic empyema, pyelitis, osteomyelitis, tuberculosis of the lungs, intestines, bones and joints, syphilis of bones, should, therefore, be as prompt as possible, and the decision as to the time and character of operation or other therapy should always be reached, with due weight being given the possibility of the occurrence of amyloid, or the influence of such treatment upon amyloid already existing. Fresh air, sunshine, and plenty of nourishing food are indicated as well for the original disease as for the anemia and cachexia attending the amyloid. Tonics are often of value. Iron and arsenic are indicated, and may be given in any form desired. Blaud's mass with arsenic is an excellent combination. The syrup or the pill of the iodide of iron may also prove useful. Potassium iodide is, of course, helpful if the lesions of late syphilis are present. Vomiting and diarrhoea will demand care as to diet and probably the use of various remedies, such as bismuth, tannigen, or even opium. But each case must be judged on its own merits, after all that is possible has been done in the way of removing or improving the fundamental and original disease.

<sup>1</sup> *Berlin. klin. Woch.*, 1885, p. 813.

<sup>2</sup> *Virchows Archiv*, vol. lxxviii.

<sup>3</sup> *Albuminuria and Bright's Disease*, p. 247



## CHAPTER XVII

### PYOGENIC INFECTIONS OF THE KIDNEY, URETER, AND PERIRENAL TISSUES

By THOMAS R. BROWN, M.D.

It seems well to consider in one chapter the various pyogenic infections of the kidney and its pelvis—pyelitis, pyelonephritis, suppurative nephritis, suppurative pyelonephritis, pyelonephrosis, pyonephrosis, abscess of the kidney, and empyema of the renal pelvis. In the first place, the etiological factors are very similar, the same bacteria may be the primary cause, and the same predisposing factors may prepare the soil; in the second place, it is very difficult to differentiate the various forms of inflammation, as they so often occur together, one often causing another and fusing imperceptibly into it, while in the third place, any of these may arise by bacteria reaching the kidney or its pelvis by any one of the usual three routes—ascending or urogenous infection, metastatic, descending or hematogenous infection, or infection by continuity from some adjacent focus of inflammation.

*Pyelitis* signifies an inflammation of the renal pelvis and its calices; *pyelonephritis*, where with this there is associated an inflammation of the kidney substance itself; *suppurative pyelonephritis*, *pyelonephrosis*, or *surgical kidney*, a suppurative inflammation of the kidney and its pelvis, associated with miliary or with larger abscesses in the kidney substance, and usually due to an ascending infection from lower portions of the urinary tract; *suppurative nephritis*, an inflammation of the kidney substance, usually hematogenous, traumatic, or by contiguity with the formation of miliary abscesses; while if we have one or several abscesses of larger size, usually due to the confluence of miliary abscesses, the condition is known as *abscess of the kidney*. In all cases of suppuration of the kidney, especially in the ascending forms, in which there is constriction of the ureter or other obstruction to the flow of urine, we get a *pyonephrosis*, if the condition lasts for any considerable period, in which there is stagnation of urine and pus in the renal pelvis and its calices, causing destructive changes in the renal parenchyma and its subsequent conversion in many cases into a pus-filled sac, pyonephrosis differing from pyelonephritis merely in the degree of distension met with. Küster speaks of this form of pyonephrosis as *empyema of the renal pelvis*, while according to this author it is best to confine the term pyonephrosis to the infected hydronephrosis, under which heading this special form of infection will be considered. In almost all cases in which the renal pelvis is diseased we meet with involvement of the ureter and its surrounding tissues, ureteritis and peri-ureteritis, leading frequently to subsequent constriction of the ureter and secondary pyonephrosis,

while in cases of inflammation of the kidney substance, especially those in which the cortex is most affected, we may have an inflammation of the tissues surrounding the kidney, perinephritis, epinephritis, and paranephritis. The pyelitis consecutive to inflammations of the kidney substance is of minor importance in the majority of cases, although, on the other hand, the renal inflammations which follow pyelitis are of very great significance, almost always being associated with far more serious symptoms and a much worse prognosis than the pyelitis itself.

By careful examination many cases of pyelitis can be diagnosed and cured before the kidney substance is involved; many cases of infection of the kidney and its pelvis will be avoided by the prompt recognition and the appropriate treatment of the antecedent causes; surgical interference, if necessary, will be inaugurated early, instead of as a last hope, and the mortality figures will be correspondingly lowered.

The great advance in our knowledge of the infections of the urinary tract has come, in part, from the development of better surgical methods, in part from more careful clinical studies, but in the main from the advances made in the field of diagnosis of diseases of the urinary tract—an advance so marked that in many diseases our whole conception of the underlying pathological process has undergone a complete change. From the clinical side, the introduction of the cystoscope has done much, but even more valuable has been the information derived from the catheterization of the ureters, by which the study of the urine from each kidney has been rendered possible. The laboratory has done its share by determining the bacteriological flora of the infections of kidney, ureter, bladder, and urethra, and by determining with a considerable degree of precision the functional ability of each kidney, of paramount importance when operation is under discussion.

Many diseases of the kidney are never diagnosed because a systematic urinary examination is neglected; if this is done in every case, many of the vague diseases, especially in childhood, would be recognized as referable to inflammations in the urinary tract; indeed, we feel that there are certain questions which should be asked in every case presented to us: Are we dealing with a healthy or a diseased kidney? If pathological, what is the nature of the disease, and what are the etiological factors? Are both sides affected or only one, and if unilateral which side is diseased? In cases of unilateral inflammation, if operation of any kind is under discussion, can the other kidney successfully perform the necessary functions? If both kidneys are involved, one more than the other, is life possible with the less diseased kidney if it is desirable to remove the more diseased organ?

**Methods of Examination.—Cystoscopy.**—The use of the cystoscope has added largely to our knowledge of urinary infections. Cystoscopy is an extremely simple procedure in the female. It may be done with the patient in the knee-chest position, or in the dorsal position with or without elevation of the pelvis; many cystoscopes are used, but no better instrument for the purpose has been devised than that of Howard Kelly. In the male the procedure is somewhat more difficult, but still comparatively easy. The strictest asepsis is essential in either case;

while, as a rule, anesthesia is not necessary, it may be required in very neurotic patients, or in case of a very irritable bladder or urethra. Berkhardt and Polano distend the bladder with pure oxygen, as they believe it has a distinctly anesthetic effect.

Besides giving a perfect picture of the condition of the bladder, its irritability or lack of irritability, its condition of distension or contraction, the presence of residual urine, foreign bodies, tumors, calculi, or communications with abscess cavities or with neighboring viscera, it also furnishes knowledge of great value as to the condition of the kidneys. The ureteral orifices can be carefully examined and deviations from the normal noted. The orifice may be gaping, invisible, or œdematous, as frequently seen in cases of calculus in the lower portions of the ureter, or it may be surrounded by an area of ulceration, as frequently seen in renal tuberculosis, while the discharge of pus or blood from the ureter may be recognized, and by this means the nature and site of the disease suggested, if not absolutely determined. It is also important to note the flow from each ureter; while normally, after the discharge of the first few cubic centimeters, the urine flows intermittently, in certain cases of hydronephrosis and pyonephrosis there is a continuous flow until the renal pelvis is emptied, and then a slow, sluggish dropping. When renal hematuria or pyuria is slight, it is difficult to make a diagnosis by cystoscopic examination alone, as the fluid from the ureter does not materially differ from that present in the bladder, while sometimes we are obliged to wait a few moments after cystoscopy to determine the character of the flow from the ureteral orifices, as the act of introducing the cystoscope occasionally produces a reflex inhibition of kidney secretion.

**Ureteral Catheterization.**—The process is somewhat difficult in the female, more difficult in the male, but it is absolutely essential in all cases of renal infection in which operation is under discussion, and most important in all other cases of suspected renal infection, for by this means alone is it possible to acquire that knowledge of the pathological anatomy and secretory peculiarities of each kidney which is indispensable to the proper treatment of this group of cases.

Some have suggested the use of catheters colored with vermilion or cinnabar lacquers, which are impermeable to the x-rays, and which are, therefore, useful in certain cases, especially in the localization of calculi; while in certain cases it is justifiable to catheterize the ureters through a bladder opened by suprapubic incision. In introducing the catheter, we can tell much regarding stricture of the ureter, and also, by the use of a wax coating, as to the presence of calculus. Kelly has shown that there may be a reflux of air into the ureter through the air-distended bladder in the knee-breast posture, while others have demonstrated that in the case of certain animals a reflux of fluids is also possible; nevertheless, it is safe to assume that the bladder is water-tight under physiological conditions, although, of course, this is not so when bladder or ureter is diseased. Rovsing puts his entire faith in the cystoscope and the ureteral catheter, and to these he ascribes his great success in nephrectomy and the reduction of his mortality in this operation from 13 to 3 per cent. since the routine introduction of these methods.



**Urine Segregators.**—The great weight of opinion is against the use of urine segregators, which were introduced because of the difficulties of ureteral catheterization. These segregators are of two kinds, each devised to obtain separate urines from the kidneys, in one type an attempt being made to form a water-tight septum between the two ureteral orifices (as in the instrument of Luys and Cathelin), in the other to elevate the posterior wall of the bladder so as to make it act as the septum (as in the instrument of Harris). Tuffier believes that this mode of examination has won a definite place for itself in the domain of renal diagnosis, while it is unquestionable that it is of value in cases in which it is impossible to find the ureteral orifices.

**The Method of Obtaining Specimens.**—It is essential that uncontaminated urine should be obtained from the bladder in the case of cystitis, and preferably directly from the kidneys in infections of that organ. Various methods have been devised for this purpose, all designed to obtain urine free from contamination. A satisfactory method is as follows in the case of the female: The vestibule of the vagina and the mouth of the urethra having been carefully cleansed with bichloride of mercury or other antiseptic solution, followed by a thorough washing off with sterile water, the lips of the urethra are pulled apart by traction on the labia, and a sterilized glass catheter with a sterilized rubber cuff about 10 cm. on its distal end is introduced, the operator only touching the rubber cuff at about its middle. After the urine has flowed for a short time, so that if a few microorganisms have been introduced from the urethra they would have been washed out, the rubber cuff is withdrawn by traction on its distal end and from 10 to 20 cc. of urine collected in a sterile tube; the same method, with slight modifications, is available in the male, a metal or rubber catheter, of course, being substituted for the glass catheter. The efficacy of this method has been shown by the fact that in fifty-two control experiments made by the writer upon normal cases, in all but one no culture was obtained, and in this one colony of a white staphylococcus grew in the plate. Some clinicians advise a thorough irrigation of the urethra beforehand with some antiseptic solution, followed with sterile water.

In obtaining urine from the kidneys, the only satisfactory method is by ureteral catheterization. In this case a cystoscope is introduced into the bladder, and through this a sterile ureteral catheter with a rubber cuff on its distal end is introduced into the ureter and inserted as far as necessary toward the renal region; if simply a study of the urine is the object, the catheter should only be inserted a distance of one to two inches in the ureter, especially if the bladder shows signs of contamination; while if we also wish to determine the presence or absence of stricture, calculus, or pyo- or hydronephrosis, the catheter must be inserted a greater distance. If there is infection of the bladder, great care should be taken; the bladder should be thoroughly washed out with some antiseptic solution, followed by repeated irrigations with sterile water; the ureteral orifice should be carefully swabbed with a solution of silver nitrate, and the catheter should be inserted but a short distance into the ureter. The success of this method is shown by the fact that in thirty-two control experiments

carried out by the writer either upon perfectly normal individuals or on those with one normal kidney, but with infection of the other, and in some cases also with cystitis, only one showed any contamination.

In obtaining specimens from the kidney, it is wise to advise the patient to drink rather copiously of water before the examination. It must be remembered that the greatest care must be taken to avoid trauma, although, notwithstanding this, chill, rise of temperature, and other symptoms may be met with occasionally after ureteral catheterization.

**Examination of the Urine.**—After having obtained the urine, it is essential that within a very short time the examination should be made. The *reaction* should be tested in every case, because it tells us in a broad way something regarding the character of the microorganisms causing the infection. Besides the mere reaction it is important in certain cases to determine the degree of the acidity, which may be done in a fairly satisfactory way by titration of the freshly obtained specimen with a decinormal solution of sodium hydroxide, phenolphthalein being used as the indicator. Of course, when the ureters are catheterized the acidity of each specimen is determined separately. It is important to determine the reaction, because, in the first place, we may meet conditions simulating a cystitis but without infection, in which the condition is due to a urinary hyperacidity, probably of neuropathic origin, and, in the second place, because certain bacteria definitely increase the acidity of the urine, others definitely decrease it. As to the normal degree of acidity, upward of 100 investigations in normal individuals showed that on the average it requires about 25 cc. of the decinormal solution to neutralize 100 cc. of urine.

The *specific gravity* should be determined because of the frequency with which a low specific gravity is met with in pyelitis and pyelonephritis, while it is especially valuable to compare the specific gravity of the urine from each kidney in cases of supposed renal infection.

The test for *albumin* should always be made, because in a broad way it differentiates vesical from renal infections. Generally speaking, there is but little albumin in the case of a pure cystitis if the fresh specimen be examined, while, in the writer's opinion, although there are many who oppose this view, there is relatively an increase of albumin in pyelitis and almost always a definite increase in pyelonephritis. Speaking broadly, a marked disproportion between the grade of pyuria and of albuminuria speaks for cystitis, while, if considerable albumin is present, pyelitis is often present alone, or associated with cystitis. Rosenfeld states that the limit of the albumin content in the severest cystitis is 0.1 per cent. in maximo, 0.15 per cent.; in pyelitis it is often 0.3 per cent., while Goldberg, who counted the red-blood cells and determined the albumin quantitatively, concluded that if the ratio of the latter amount in percentage to the number of red corpuscles per cmm. is more than 1 to 30,000, there is true albuminuria, while if less than 1 to 30,000, the albumin is accounted for by the blood alone.

The *microscopic examination* is of extreme importance and should be made with great care. The centrifugalized specimen should be examined, and at the same time, by allowing a definite quantity of urine

to stand a certain time, we learn something regarding the degree of infection, and the effect of any treatment we are employing may be roughly judged by the depth of this sediment. Special attention should be paid to the presence or absence of *microorganisms*, *casts*, *pus cells*, *red-blood cells*, and *epithelial cells*. As to the *microorganisms*, their number, motility, and morphology should be noted; stained specimens should always be made, and in every case in which there is the least suspicion of such infection, tubercle bacilli should be stained for; in cases in which bacteria are seen microscopically but the cultures are sterile, it is extremely important that anaërobic cultures be made. In case of *blood* in the urine, the only way to exactly determine its source is by cystoscopy and ureteral catheterization. As regards *pus cells*, ureteral catheterization is essential in determining their source. The claim some make, that certain *epithelial cells* are peculiar to the pelvis of the kidney and the ureter, is erroneous, because exactly similar cells may be met with in the lower epithelial layers of the bladder, and consequently are found in cases of pure cystitis. As a criterion of the effect of any treatment, the number of pus cells and red-blood cells can be counted from time to time with a hematocytometer.

**Functional Activity of the Kidneys.**—Within the past few years methods to determine the functional activity of the kidneys have been most carefully studied. These functional tests have proved of great value in making the prognosis of various renal diseases, but have perhaps their widest application in deciding the question whether or not operation is justifiable in various surgical diseases of the kidney. In the former case the mixed urine from the two sides has been studied, as a rule, while in the latter the more valuable findings are the functional activities of the separate kidneys determined by ureteral catheterization, and the comparison of the urine obtained from the separate sides.

Many methods have been employed, such as the determination of the urea and of the total nitrogen in the twenty-four hour specimen, cryoscopy of the blood and urine, the study of the elimination of various colored substances by the urine, these usually being administered hypodermically, the tests of the electrical conductivity of the urine, the determination of its toxicity, of the amount and specific gravity of the specimens from the two sides, and the flexibility of its reaction to large quantities of water administered by mouth, the chloride elimination, and also the rate of elimination of lactose, potassium iodide, and other substances administered by mouth, as well as the quantitative estimation of the ferments found in the urine, notably diastase, and the quantitative estimation of the incoagulable nitrogen in the blood. In all cases of renal disease, and especially when operation is under consideration, it is of paramount importance to determine as far as it is possible the functional activity of the kidneys, especially after catheterization of the ureter, and the comparison of the urine from the two sides. For general purposes the phenolsulphonaphthalein test as a criterion of general functional activity, the lactose test for the study of glomerular, and the potassium iodide or sodium chloride estimation for the study of tubular changes are possibly of most value, although there is no



substance which is excreted entirely by glomerular, or entirely by tubular epithelium. Information of great importance can also be furnished by the determination of the incoagulable nitrogen in the blood. While on test is infallible, nevertheless by these functional tests information of great value may be obtained, although it is needless to say it must always be correlated with the clinical findings.

**Bacteriology.**—Certain things should never be forgotten in making bacteriological examinations of the urine: first, the necessity of examining for the tubercle bacillus by the ordinary methods, and by animal inoculation in all doubtful cases, especially when the urine is acid and shows no growth on the ordinary culture media; second, the necessity of making anaërobic cultures, if bacteria are seen in the stained centrifugized specimens and no growth occurs on the ordinary media.

**The Bacteria of the Normal Urethra.**—It is essential to consider these, because one of the common causes of cystitis is the introduction of some of these bacteria into the bladder by a catheter or other instrument. We may safely say that all the mucous membranes in contact with the air contain bacteria, and of these some will be pathogenic. Melchior found the colon bacillus in the vulva of healthy women in half those examined; Bouchard and Charrin found this microorganism frequently in this location, and it is probable that in a large number of cases the colon bacillus as well as other pathogenic bacteria are to be found in the vulva and the vestibule of the vagina in women and on the glans in the male. As to the bacterial flora of the normal urethra much work has been done, and the results in the main have harmonized. All investigators have found many varieties of bacteria in the healthy urethra in both the male and female, including staphylococci and streptococci. Melchior found that only after very careful irrigation with boracic acid solution and subsequent catheterization could he obtain a urine free from bacteria. Kraus and Chvostek found bacteria in the urethra at a depth of 6 to 8 cm. in 60 per cent. of healthy males examined by them, while Schenk and Austerlitz found the urethra free in more than half the cases of normal women.

The following bacteria have been found in the urethra: The colon bacillus, *Staphylococcus pyogenes aureus* and *albus*, various forms of streptococci, *Diplococcus candidus*, various forms of sarcina, leptothrix, *Streptococcus liquefaciens*, pseudogonococcus, smegma bacillus, pseudodiphtheria bacillus, *Diplococcus pyogenes*, and many others. Of the pathogenic forms, such as the colon bacillus or staphylococci—in other words bacteria which can cause cystitis—Melchior has shown that they are present in more than half of the normal urethras. These results show the importance of the urethra as a source of infection of the urinary tract, and accentuate the necessity of extreme care in introducing catheters and other instruments.

**Urethritis.**—Although the gonococcus is the cause of infection in the vast majority of the cases, we may have a urethritis due to other forms of bacteria, as the experimental urethritis brought about by the introduction into the urethra of various bacteria, especially various forms of staphylococci and diplococci. Among other causative factors

in urethritis may be mentioned the *Streptococcus pyogenes*, *Micrococcus cereus albus*, *Bacillus coli communis*, *Staphylococcus pyogenes aureus* and *albus*, *Staphylococcus non-liquefaciens*, tubercle bacillus, etc. It is not at all uncommon as a sequel of gonorrhea to find a condition in which the urine shows numbers of organisms—bacilli, cocci, diplococci, etc.—which unquestionably tend to keep up inflammation.

**Cystitis.**—The bacteriology of infections of the bladder has for obvious reasons been studied far more thoroughly than the infections of any other portion of the urinary tract. Before taking up the findings in cystitis it will be well to discuss certain questions of importance in this connection, such as the mode of entrance of the bacteria, the predisposing causes of infection, and other etiological factors.

As regards the *mode of entrance* of infection in the bladder, this may be through the urethra either from the organisms usually present, or from bacteria present on an instrument used; we may have a descending infection from the kidney; we may have an infection by direct transmission from the intestinal tract; we may have an infection carried by the blood stream to the bladder, or a direct extension from some inflammatory focus localized in the pelvis or the lower portion of the abdomen. Examples of all of these modes of infection occur, but infection from the urethra, from instrumentation, or from direct extension are those most commonly met with. Infection from the intestine is especially liable to occur if there is a slight lesion or congestion of the intestinal wall, as in diarrhea or after other intestinal disturbance.

In looking over the bacteriological findings in cystitis one is at once struck by the fact that in a great number of cases microorganisms are found which, as a rule, possess but slight pathogenic properties, and it would, therefore, seem probable that other etiological factors play an important part in the causation of cystitis. The function of the bladder epithelium is purely protective, and it is still a moot question whether absorption is possible from the healthy bladder. However, it has been shown by many investigators that infection occurs if the bladder mucous membrane be harmed or the urethra ligated, although in the case of *Bacillus proteus*, which decomposes the urine and renders it alkaline or ammoniacal, no other factor seems necessary. Melchior also found in rabbits that although bacteria introduced into the healthy bladder did not produce cystitis, yet an inflammation could be set up by the application of cold to the pubic region, by the injection of hot or cold water, or by artificial trauma, results similar to those obtained by Bumm in the case of the gonococcus and by Rovsing with a large number of bacteria.

Among the more important factors which predispose to cystitis may be mentioned an ammoniacal urine usually due to the *Bacillus proteus* or other urea decomposing bacteria, various conditions which interfere with the bladder function and tend to impair its vitality, such as injuries and diseases of the nerves of the bladder, as in paraplegia and myelitis, congestion of the mucous membrane, especially the trigonal area, pressure, or obstruction to the flow of urine, pregnancy, excessive cold or heat, anything that prevents a complete emptying of the bladder,

injury or trauma to the bladder, due to instrumentation, catheterization, operation or calculus, adhesions between the bladder and other organs, neoplasms, and conditions which lower the resistance of the body.

Pasteur, in 1859, suggested that bacteria were the cause of urinary decomposition, but it was not until 1887 that Clado isolated his *bactérie septique de la vessie* as the cause of cystitis, and the same year Hallé described a short non-liquefying bacillus as the cause, which Albarran and Hallé found in 47 of 50 cases of urinary infection, calling it *bactérie pyogène* and producing cystitis in animals by its introduction if the urethra was ligated. This bacterium was found later to be identical with the colon bacillus. Clado's *bactérie septique*, Krogius' *bacille non-liquefiant*, Morelle and Deny's *Bacillus lactis aërogenes* probably, and Rovsing's *Coccobacillus ureæ pyogenes* are all probably varieties of the colon bacillus, while the *Bacterium vulgare* and the *Urobacillus liquefaciens septicus* are identical with the *Bacillus proteus vulgaris* of Hauser. Marked polymorphism as regards motility and cultural peculiarities may be produced in the colon bacillus by variations in the culture medium and environment, and also marked changes in the staphylococcus as regards grouping and chromogenic properties appear under similar conditions; it is, therefore, not at all surprising that a large number of different bacteria and cocci have been described.

Albarran, Hallé, and Legrain, in 1898, collected 304 cases from the literature, and found in 131 the colon bacillus 89 times in pure culture; other microorganisms found were *Bacillus proteus*, *Streptococcus pyogenes* (18 times), gonococcus and tubercle bacillus, while among the less common findings were the typhoid bacillus, the diplococci of Fränkel and of Friedländer, *Bacillus longus ureæ*, *Bacillus crassus*, streptobacillus, urobacillus, coccobacillus, *Micrococcus subflavus*, and *Sarcina alba*, *Bacillus lactis aërogenes*, *Streptobacillus anthracoidis*, yeast, various diplococci, the pseudodiphtheria bacillus, the *Bacillus pyocyaneus*, influenza bacillus, *Filaria sanguinis hominis*, bilharzia, echino coccus, various forms of yeast, and *Amæba coli*. In recent years many have called attention to the frequency with which cystitis due to the colon bacillus occurs in children.

Melchior, in 72 cases, found the colon bacillus 37 times (29 in pure culture); *Streptococcus pyogenes* in 4 (3); proteus of Hauser, 10 (4); tubercle bacillus, 4 (3); *Diplococcus ureæ liquefaciens*, 14 (11); *Staphylococcus ureæ liquefaciens*, 3 (1); *Streptococcus anthracoides*, 3 (0); gonococcus, 2 (2); typhoid bacillus, 1 (1); *Staphylococcus pyogenes aureus*, 4 (3); and coccobacillus, 1 (1). He found, as the vast majority of other investigators, that in most cases the urine is acid; in fact, with the exception of the proteus and a few species of micrococci, such as the *Micrococcus ureæ liquefaciens*, the urine is invariably acid; the frequency with which Rovsing found alkaline or ammoniacal urine is probably due to the fact that a large proportion of his cases were in old men with enlarged prostate, while Schnitzler's high percentage of alkaline cases is due to the fact that most of them were in cases of malignant disease, in which the proteus bacillus seems to thrive peculiarly well. Moullin, in 30 cases of cystitis, found the urine acid or neutral in 24, alkaline in 6; he found



the colon bacillus 25 times (14 in pure culture), proteus bacillus 5 times, and the *Streptococcus pyogenes* 7 times.

Albarran and Cottet found one species of bacillus and two of cocci in anaërobic cultures, a very important finding and one that should suggest the advisability of making anaërobic cultures much more often.

Personal researches into the bacteriology of cystitis, published in 1899, showed in 26 cases of acute cystitis the colon bacillus in 15, the *Staphylococcus pyogenes albus* in 5 and *aureus* in 2, *Bacillus pyocyaneus*, typhoid bacillus, proteus bacillus, and an organism resembling in many respects the colon bacillus, 1 each, while in chronic cases the bacteriological findings were tubercle bacillus in 6, colon bacillus in 16, *Staphylococcus pyogenes aureus* in 3 and *albus* in 2, a bacillus resembling the colon bacillus in 1, the white staphylococcus, which decomposes urea, in 4, *Bacillus proteus* in 1, while in 2 cases the cultures, both aërobic and anaërobic, were negative. The comparison of the bacteria found in the acute and chronic cases shows no greater prevalence of the colon bacillus in the chronic than in the acute cases, which is important in that certain investigators claim that the colon bacillus frequently enters after the development of cystitis and drives out the other bacteria. In these cases the microörganism was met with in pure culture in all but one of the cases, in which case the colon bacillus and the tubercle bacillus were associated. In the 60 cases of cystitis in which bacteria were found, the colon bacillus was found in 31, the *Staphylococcus pyogenes albus* in 7, tubercle bacillus in 6, the *Staphylococcus pyogenes aureus* in 5, the white staphylococcus, which decomposes urea, in 4, proteus bacillus in 2, and the typhoid bacillus, pyocyaneus bacillus, and unidentified bacillus, resembling in many respects colon bacillus, in 1 each. The urine was acid in the case of all the *bacilli* except *Bacillus proteus*, was generally acid, occasionally neutral, and very rarely slightly alkaline in the case of the *Staphylococcus pyogenes albus* and *aureus*, and alkaline or ammoniacal in the case of the white urea-decomposing staphylococcus and the *Bacillus proteus*. This series of cases consisted exclusively of women, and a comparison of the results found by others shows that the colon bacillus is somewhat more prevalent in women than in men, while the less common forms are more likely to be found in men.

**Ureteritis**—This is practically the same as cystitis on the one hand and pyelitis on the other, for in the vast majority of cases the ureter becomes infected either from an ascending infection from the bladder or from a descending infection from the renal pelvis. In exceptional instances the ureter may become infected from some contiguous focus of inflammation, and cases have been reported in which a ureteritis has directly followed an acute appendicitis or an appendicular abscess. The ureteral epithelium is, like that of the bladder, very resistant to infection, and unquestionably many bacteria may pass down the ureter, if in a healthy condition, without setting up inflammation. If, on the other hand, the ureter is not normal, but is congested, dilated, or constricted, due to pressure, as from the pregnant uterus, or is diseased because of contiguous disease, its chance of infection is markedly increased.

**Pyelitis, Pyelonephritis, and Infections of the Kidney.**—Most of the tables of the bacteria found in pyelitis are of very little value, because the urine has been obtained from the bladder and not directly from the kidney by ureteral catheterization. Within recent years this latter method has been used and, although the number of cases is comparatively small, nevertheless we know the microorganisms most likely to be found in infections of the renal pelvis or of the kidney itself. As to the source of infection, we may have an ascending infection from the bladder up the ureter, the kidney may become infected from the intestinal tract, the bacteria being carried by the blood or by the lymph current; infection of the kidney may be but a part of a general infection, or bacteria may be carried from some nearby focus of infection, such as an abscess cavity, by the blood or lymph current, or by direct extension.

The bacteria found in our series of 20 cases of pyelitis and pyelonephritis in which the urine was obtained by ureteral catheterization, were as follows: Of 3 acute cases, in 2 with acid urine, bacillus coli was found once and the tubercle bacillus once, and in the 1 case with alkaline urine bacillus proteus; of 17 chronic cases, in 12 with acid urine the colon bacillus was found in 6, the tubercle bacillus in 5, and in 1 case no bacteria were found, while in 5 cases of alkaline urine the proteus bacillus was found in 3, and the white urea-decomposing staphylococcus in 2 cases. In all the chronic cases with alkaline urine a stone was found in the renal pelvis, and in several cases in which cultures were made from the centre of the stone the microorganism was found which was the cause of the pyelitis, suggesting that the cause of stone formation is primarily a mass of agglutinated bacteria about which the salts precipitated in the alkaline urine are deposited. In each case, both acute and chronic, the microorganisms were present in pure culture.

The presence of accessory factors is far more difficult to determine in the kidney than in the bladder, but the fact that the condition is more likely to occur in people who are run down, anemic, or depleted by various diseases, or in whom there is a condition of stasis of urine due to pressure upon the ureter by a tumor or pregnant uterus, or by constriction of the ureter due to adhesions, or in whom the kidney is congested, suggests that here also accessory factors play an important part. Why one kidney should be affected and not the other is in most cases impossible to say, but it is suggestive that in two of this series the kidney affected was markedly displaced. As to the mode of infection, in 6 cases of this series the infection was undoubtedly ascending, and in 7 hematogenous as far as one could tell; in the tuberculous cases 2 were unquestionably hematogenous in origin, while in the other 4 it was impossible to tell, although clinically the bladder symptoms made their appearance first. The study of these cases suggested that if the kidney became infected first the bladder as a rule showed fewer lesions than if the bladder was affected first and the kidney secondarily.

Albarran, Tuffier, Schmidt, Aschoff, and Savor have shown the importance of the colon bacillus in infections of the upper urinary tract, while Melchior has shown that, if the colon bacillus is injected into the bladder and trauma produced or retention caused, in addition to the cystitis he

could produce pyelitis, pyelonephritis, abscess of the kidney, and suppurative nephritis, and that in certain cases the colon bacillus was even found in the circulating blood. Von Albeck has called attention to the frequency with which the colon bacillus is found in the urine of pregnant women.

**Bacteriuria.**—This is the condition in which the urine becomes infected without any demonstrable lesion of the urinary tract. The epithelium of the urinary tract is extremely resistant to infection. In addition, the normal urine possesses very distinct bactericidal properties, as Lehmann, Richter, Rostoski, and others have shown, largely dependent upon the degree of acidity which the urine shows. Whether the normal urine does or does not contain bacteria has always been a matter of discussion, many investigators holding that it does not, while many others contend that it does. The weight of evidence certainly points to the belief that the urine of healthy individuals, if obtained under careful precautions, contains no bacteria, and in 88 observations on healthy human beings the writer did not find bacteria in the urine in any case.

In infectious diseases, however, unquestionably bacteria can be found in the urine, as in typhoid fever, in which the bacilli are found in the urine in from 20 to 40 per cent. of the cases, tuberculosis, where either the tubercle bacillus or various cocci have been found, anthrax, plague, and various localized infections due to staphylococci or streptococci. The fact that most observers have found traces of blood and albumin in the urine in association with the bacteria in these cases, and also in experimental injections of bacteria into the blood, suggests that in all probability the bloodvessels of the glomeruli undergo certain pathological changes before the bacteria can penetrate them. Nevertheless, according to Orth and Baumgarten the kidneys are permeable when lesions cannot be made out by microscopic examination, while Biedl and Kraus have shown that after the injection into the blood of various bacteria, within a few moments these same bacteria may be found in the urine without blood or albumin.

In the vast majority of cases of bacteriuria the source of the bacteria is undoubtedly the gastro-intestinal tract, for it has been shown that even a slightly altered intestinal mucous membrane is pervious to bacteria; as a rule, ordinary constipation is not enough to allow this permeability, but if it is prolonged or associated with lesions of the mucous membranes, even though very slight, bacteria may reach the blood or lymph streams, and be carried to the kidney or the bladder, as the case may be, setting up a bacteriuria either of renal or of vesical origin.

As to the bacteria found in bacteriuria, the colon bacillus is met with in the vast majority of cases, but other bacteria have been found, such as the typhoid bacillus, various streptococci and staphylococci, sarcina, *Bacillus lactis aërogenes*, and in rare cases even the *Bacillus proteus*.

**Conclusions.**—There are certain other questions which should be touched upon. It is important to remember that the epithelium of this tract is extremely resistant to infection, and that in the vast majority of cases certain predisposing factors must be met with before inflammation is set up. It is probable that in men spontaneous infection of the bladder from the urethra does not take place, probably due to the internal sphincter,



while in women it unquestionably may occur, although in the great majority of cases instrumentation or some other condition which lowers the resisting power of the bladder precedes it. While entirely possible for a regurgitant blood-stream to carry bacteria from the urethra to the bladder, and even from the bladder to the kidney, these methods of infection must be rare. Under very slight pathological conditions of the intestinal tract, bacteria, especially the colon bacillus, may penetrate the intestine and enter the blood and lymph streams, to be carried thence to the kidney and bladder.

As to the constitutional effects of pyelitis, cystitis, etc., these depend largely upon the amount of absorption, and this in turn is dependent on the extent of injury which the epithelial layers have undergone. Thus, in acute cystitis there is considerable absorption, because the superficial cells are rapidly destroyed and the absorption of the poisons formed is rendered easy; obviously, if anything prevents the free flow of urine from the renal pelvis or bladder, the chances of absorption are markedly increased. In chronic cystitis the constitutional symptoms are less, as a rule, because the covering of pus, mucus, etc., over the ulcerated surfaces usually renders absorption slight. As to the poisons which cause these constitutional effects, the only ones carefully studied have been those formed by the colon bacillus in its growth; indol and two ptomaines, putrescin and cadaverin, have been described.

The use of the *agglutination test* in diagnosing these infections of the urinary tract has been used in a number of instances, although it must be remembered that when dealing with the same bacterium agglutination will only take place with a homologous strain. Of course, in all cases we may either use precipitation tests, the thread reaction, Pfeiffer's phenomenon, or the ordinary agglutination test.

**Etiology.**—To get a proper conception of the various inflammations of the kidney and its pelvis it is absolutely essential to understand the causative factors involved, both the primary causes and the accessory factors. Practically all forms of inflammation of the kidney are due to bacteria, but in many cases, probably the majority, other factors must be present before infection occurs. In certain cases we may have a pyelitis or pyelonephritis due to various poisons and drugs, or to the toxins produced in various diseases. Under normal conditions the kidney and its pelvis shows marked resistance to infection; bacteria of various kinds have been injected into the circulating blood and into the bladder, but no infection has occurred in many cases unless some trauma or impediment to the flow of urine has been artificially produced. In many infectious diseases bacteria may pass through the kidneys without producing any permanent lesion. In some cases there is a true renal bacteriuria, in which the urine becomes infected without involvement of the kidney, and contains many bacteria, usually colon bacilli, but no pus cells; although, if stasis of urine occurs, or the resistance of the kidney is lowered, pyelitis or a renal infection may arise. The degree of infection in the individual case depends to a certain extent upon the number, virulence, and character of the bacteria and their mode of entrance, but far more in the majority of cases upon various

accessory factors which make the kidney a *locus minoris resistentiæ*, be those causes local or general.

**Bacteriology of Pyelitis, Pyelonephritis, and Suppurative Inflammations of the Kidney.**—A great variety of bacteria has been found in these conditions, much the same flora, in fact, as that met with in cystitis, although the relative frequency of the different species is quite different. Among the organisms found may be mentioned *Staphylococcus pyogenes aureus* and *albus*, *Streptococcus pyogenes*, *Diplococcus ureæ liquefaciens*, a urea-decomposing white staphylococcus, pneumococcus, *Bacillus proteus vulgaris*, typhoid and colon bacilli, *Sarcina flava* and *alba*, diphtheria bacillus, gonococcus, influenza bacillus, and various rare bacteria, the microörganisms being usually found in pure culture, although occasionally a mixed infection is met with. In all cases in which the microscope reveals bacteria, but nothing grows on the ordinary media, one should make anaërobic cultures, or at least use special staining reactions, while in all cases in which there is any doubt as to the etiology, especially if associated with an acid urine, the tubercle bacillus should be carefully looked for. Lenhartz, in 80 cases of pyelitis and pyelonephritis, most of which developed during or after pregnancy, found the colon bacillus 66 times in pure culture, paratyphoid bacillus 3 times, *Bacillus lactis aërogenes* twice, *Bacillus proteus vulgaris* twice, and Friedländer's pneumobacillus once. Von Albeck in 92 cases of pyelitis and pyelonephritis in pregnant women found the colon bacillus 76 times in pure culture, and 3 times with pyogenic cocci, staphylococci alone 4 times, and streptococci alone 9 times.

Rovsing found that the bacteria in men and in women differed in this ratio: in 18 cases in women the colon bacillus was found 16 times in pure culture, once with the *Streptococcus ureæ*, and the *Streptococcus pyogenes aureus* once in pure culture; in 14 cases in men the colon bacillus was found 5 times, *Staphylococcus pyogenes aureus* twice, *Staphylococcus pyogenes albus* twice, *Bacillus liquefaciens* once, *Bacillus longus liquefaciens* once, *Sarcina flava* once—all in pure culture—while in one case *Staphylococcus pyogenes albus* and *Streptococcus pyogenes* were found, in another *Bacillus proteus vulgaris* and staphylococcus. In a series of 14 cases, 13 women and 1 man, observed by the writer, in all of which both kidneys were catheterized separately, the colon bacillus was found 8 times, *Bacillus proteus vulgaris* 3 times, a white staphylococcus, which decomposed urea but did not liquefy gelatin, twice; while in one, a case of thirty years' standing, no growth occurred, the bacteria evidently having died out. In all cases the bacteria were found in pure culture. According to Küster, the colon bacillus is the cause of the infection in at least one-third of the cases of suppurative nephritis, while Guyon and many others have stated that in their experience the colon bacillus is the commonest cause of all the infections of the urinary tract. As to the bacteriology of bacteriuria, although the colon bacillus is present in the vast majority of cases, *Bacillus lactis aërogenes*, *Staphylococcus pyogenes aureus* and *albus*, *Streptococcus pyogenes*, *Bacillus typhosus*, *sarcina*, and even *Bacillus proteus vulgaris*, have also been described. That the organs and urine of absolutely normal individuals are free from

bacteria has the weight of authority, and thus, at the present time at least, it is not fair to assume that we may have autogenous infections of the kidney. Whether the gonococcus of itself can cause infection of the kidney is still under discussion, although it is difficult to explain certain cases on other grounds. Certainly its virulence is slight, and when the predisposing causes are removed a rapid cure occurs in the majority of cases.

**Paths of Entry of the Bacteria.**—In each case we must determine whether the infection is hematogenous, urogenous, by contiguity, or by the medium of a penetrating wound. *Hematogenous* or *metastatic* infection may occur in any condition in which bacteria may get into the circulating blood. In regard to the commonest cause of renal infection, the colon bacillus, it has been very definitely shown by Posner, Lewin, and others that a pathological intestinal wall is pervious to bacteria, and that although ordinary constipation (from one and a half to two days) is not sufficient, longer constipation or surprisingly slight lesions of the mucous membranes allow the bacteria to enter the circulating blood; it has also been shown that the virulence of this bacillus is markedly increased in diarrhoea and other intestinal diseases, and this probably explains why in some cases it does no harm in its transit, while in others it may produce all grades of infection from a simple bacteriuria to a suppurative pyelonephritis.

The *urogenous* or *ascending* infection is peculiarly interesting, especially because infection of the kidney so commonly follows that of the bladder, although there is still some question as to exactly how this occurs. The commonest cause of cystitis unquestionably is instrumentation, the catheter or other instrument often producing trauma, and introducing bacteria if the technique is faulty, while a study of the bacterial flora shows that it is quite possible for cystitis to arise from that source; in men it is improbable that spontaneous infection of the bladder from the urethra occurs, but in women this source is undoubted.

It is a moot question whether Petit's old view that under normal circumstances no escape of the urine from the bladder into the ureters is possible because of the oblique course of the latter in the vesical musculature is supported by the facts. Lewin and Goldschmidt showed that this is not so in the case of rabbits, while Guyon and Courtade demonstrated that this reflux is far less likely to occur in dogs in which the bladder muscle is stronger. Sampson and Young found that considerable distension of the bladder in dogs, or in the cadaver, was possible without any fluid entering the ureter. Although Kelly showed a reflux of air from bladder to ureter, nevertheless it is highly probable that in the vast majority of cases in health no reflux of fluid occurs even with considerable distension. In disease such a reflux undoubtedly does occur. Sampson showed that bacteria may be carried from the bladder to the kidney by the general circulation, the vesico-ovario-renal anastomosis, the blood-vessels of the ureter (all of these being examples of hematogenous infection), the lymphatics, or by the lumen of the ureter.

We may unquestionably have *direct transmission* of bacteria by way of the lymphatics from the colon to the kidney, especially on the right side,



where the organs are in such close proximity, and this is peculiarly liable to occur in cases of nephroptosis. Whether urogenous or hematogenous infections are most common is undecided. It seems unquestionable that when the renal pelvis is affected first the infection is more likely to be urogenous, while, in inflammations beginning in the kidney substance itself, hematogenous infection is more common.

**Accessory Factors.**—While bacteria are always the primary cause except in those rare cases in which inflammatory changes are produced by various drugs, poisons, and toxins, nevertheless in most cases other factors are involved without which the infection would not take place; although in the case of renal infections it is far more difficult to determine these predisposing causes than in the case of infections of the bladder. Certain bacteria, especially if very virulent, if present in very large numbers, or if they have the power to decompose urea, thus producing substances irritating to the renal pelvis, may cause infection with no adjuvant causes. Most of these accessory factors act either by lessening the general strength of the patient, by lowering the resistance of the kidney, by trauma, or by causing retention and stasis of the urine. The importance of this last factor has been determined, and stricture and encroachment upon the lumen of any portion of the urinary tract are among the most potent predisposing factors.

Among the accessory factors may be mentioned: Various *general* and *local infections*; marked *constipation* and *gastro-intestinal disease*; *calculus*, although stone is more likely to be caused by pyelitis than the reverse; *diseases of the kidney*, such as the various forms of nephritis; *cystitis*, this in older people almost always associated with retention, and if long continued almost always leading to pyelitis or pyelonephritis; *stricture of the ureter* or of the *urethra*, *narrow urinary meatus*, and *phimosis*, these causing retention of urine, and the two former frequently causing not only pyelitis and pyelonephritis, but also pyonephrosis or empyema of the renal pelvis; *wounds* of the kidney or its pelvis; *trauma*, frequently associated with small hemorrhages or tears in the kidney substance, or in the perinephric tissues; *chronic passive congestion*; some *near-by focus of inflammation*, such as acute appendicitis, pelvic peritonitis, etc.; *nephroptosis*, or floating kidney, *hypertrophy of the prostate*, the pressure of *tumors*, *inflammatory exudates*, the *pregnant uterus*, and possibly the *distended colon* upon the ureter, and the constriction of the ureter, due to *adhesions* or consecutive to *ureteritis* and *periureteritis*; *anemia*, *unhygienic mode of life*, or *malnutrition*, *intercurrent disease*, or anything which may lower the general resistance; various *parasites*, such as *actinomyces*, *Eustrongylus gigas*, *filaria*, *echinococcus*, *bilharzia*. *Tuberculosis of the kidney* is sometimes followed by secondary infection with one of the pyogenic bacteria, as also *paralysis of the bladder* from injury or disease of the spinal cord, etc. *Gonorrhœa* probably sometimes causes infection of the kidney, but is more often followed by a secondary infection due to other bacteria. The use of *instruments* may not only produce trauma, but also introduce bacteria. *Holding urine for a long period of time voluntarily* may be a cause. *Injuries* to the *rectum* or the mucous membrane of any portion of the *gastro-intestinal tract* may

allow bacteria to enter the blood-stream, and *cold*, possibly by lowering the resistance of the kidney, has been mentioned, although it is questionable whether this is really contributory.

In metastatic forms of renal infection the disease is usually bilateral, while in the cases due to trauma or to contiguity, unilateral infection is the rule. In ascending or urogenous infections it is far more often unilateral. In our series of 14 cases of pyelitis and pyelonephritis, 7 of which were urogenous, 6 hematogenous, and 1 by contiguity, 13 were unilateral, 1 bilateral, and of the unilateral the right side was affected in 8, the left side in 5 cases. Other series give a far greater relative frequency of involvement of the right side than the left; the proximity of the right kidney to the colon and its tendency to ptosis may have something to do with this increased susceptibility. In all cases, if the infection has lasted for a long period, there is a tendency for the other kidney to become infected usually by way of the bladder, although in some cases it is remarkable how long one kidney may remain intact with advanced disease of the other, and even with cystitis. In the suppurative inflammations bilateral infection is more common than unilateral.

As to *age*, pyelitis and pyelonephritis are met with in children, even in very young infants to a considerable extent, although this has only been recently recognized, and even now in the majority of cases the proper diagnosis is not made; girls are more frequently affected than boys. In the aged the condition is common, due to the prevalence of many of the accessory factors mentioned above. The common years are between twenty and fifty, that is, the time when urethral troubles are most common in men, genital troubles in women, while it is also common in later life in men due to the tendency to enlargement of the prostate, and associated cystitis with retention.

Infections of the kidney and of its pelvis in *pregnancy* are of great importance. Von Albeck, in 7648 cases in Meyer's clinic, found pyuria in 392, and in 52 of these, that is, 14 per cent., there were signs which pointed to pyelitis or pyelonephritis. Lohlein and Olshausen have shown that the ureters are always dilated in women dying in labor, the dilatation being above the superior strait. Opitz has observed 84 cases during pregnancy and the puerperium, while Swift, who collected 41 cases, found that the right side was involved 37 times, the left side 4 times, and that of the 29 women in which the information was obtained, 15 were primiparous, 14 multiparous.

**Pathology.—Pyelitis.**—The typical pyelitis is that met with in ascending or urogenous infections, while that consecutive to renal inflammation is not likely to be so severe or to show such marked changes. In ascending pyelitis the pelvis of the kidney shows a most variable picture, according to the type of infection, its duration, its virulence, and with what accessory factors it is associated. The pelvis may not be dilated at all, may be slightly or moderately so, or if obstruction occurs below the pelvis, if persisting for some time, there may be an extreme distension.

*Acute catarrhal pyelitis* gives the typical picture of an acute inflammation; the mucous membrane is congested, swollen, and hyperemic, while on its surface may be seen red-blood cells, pus cells, a few

desquamated epithelial cells, mucus and bacteria in greater or less amounts, phosphate and oxalate crystals if the urine has been rendered alkaline, and even bits of calculus, if that is the predisposing cause. The bacteria are often agglutinated masses, and these may be the nucleus around which a stone may form, although this is almost exclusively confined to the alkaline infections. Occasionally the blood is present in larger amount, due to trauma, the effect of certain toxins, to some peculiarity of the blood, or to an increased permeability of the blood-vessel wall.

*Chronic Pyelitis.*—In this the picture is quite different. The mucous membrane is brownish or grayish red in color, discolored spots frequently mark the remains of old hemorrhages, the mucous membrane is frequently pigmented and practically always markedly thickened, while the veins are enlarged and tortuous. The covering of the mucous membrane is markedly dependent upon the nature of the infection, and especially upon whether the urine is acid or alkaline. In acid infections the mucous membrane is covered with a layer, often quite thin, and very thick only in a small proportion of the cases, consisting of mucus, epithelial cells, pus cells, usually a few red-blood cells, many bacteria often in clumps, and sometimes deposits of crystals of uric acid and urates; while in the alkaline infections the coating is much thicker, as a rule, usually mucopurulent, with a foul odor, with phosphate and oxalate crystals embedded in it. Ulceration is much more common than in acute pyelitis, and this is peculiarly so in those cases in which the urine shows ammoniacal decomposition. The ulcers are often very deep, and may in rare instances even perforate into the neighboring organs and tissues, especially the pararenal fat, leading to burrowing abscesses which may discharge externally or into a neighboring viscus, the fistulæ usually being very persistent. Various forms have been described: *gangrenous pyelitis*, *cystic pyelitis*, *granular pyelitis*, *pseudomembranous pyelitis*, and *fibrinous, croupous*, or *diphtheritic pyelitis*.

In cases of pyelitis consecutive to suppurative nephritis the pelvis is less likely to be seriously involved than in ascending infections, while in the latter cases all stages of the cysto-ureto-pyelonephritis may be of marked severity. The substances produced by the ammoniacal decomposition of the urine are peculiarly destructive to the mucous membrane, and in this class of cases the most severe forms of pyelitis are found.

The corresponding *ureter* is usually involved in cases of ascending pyelitis, although in rare instances it may be entirely normal; especially important are the changes about the ureteral openings into the bladder; and a diseased condition of the mouth of the ureter is one of the most important diagnostic signs of renal infection. The mucous membrane of the ureter may be chiefly affected (*internal ureteritis*), or the surrounding connective and fatty tissue may also be involved (*external ureteritis* or *periureteritis*). The changes in the ureteral mucous membrane are of the same character as those in the mucous membrane of the renal pelvis. The changes in the ureter are much more common in ascending infections, although frequently met with in the descending type; often in the latter case only the upper portion of the ureter is involved.



If there is obstruction in the ureter, or even in the urethra, we will get stasis of urine, and first distension of the pelvis, then of the calices. Finally, if the obstruction is not removed, the entire kidney may be destroyed and converted into a large pus sac—and thus we may get varying grades of *pyonephrosis* or *empyema of the renal pelvis*, or even *hydronephrosis*. Sloughing of the calices, or even of the entire pelvis, may occur, while frequently we have in one and the same picture the pathological changes characteristic of pyelitis, pyelonephritis, and pyonephrosis. The kidney may be converted into one large abscess or into a series of smaller abscesses separated by remains of the connective tissue, or may be converted into a fatty mass, often still containing a few pus cavities. The pus may become inspissated, calcified, or converted into a serous fluid by absorption. If the process extends through the kidney we may find inflammation of the capsule both fibrous and fatty sometimes associated with abscess formation. The gradual dilatation of the pelvis and the calices, with papillary flattening, and subsequent atrophy and destruction of the kidney substance, the medulla being affected first and the cortex afterward, is peculiar to ascending pyonephrosis, while in the descending form the ureters are less likely to be affected and the cortex shows earlier changes. In both cases the vessels in the pedicle are often of surprisingly small size.

Besides the pressure changes, the kidney may be markedly involved by an extension of the infection, and we may get a chronic interstitial nephritis, suppurative pyelonephritis, pyonephrotic changes or abscess of the kidney, with possibly hypertrophy of the other organ.

**Ascending Pyelonephritis.**—In certain cases it is surprising for how long a period of time the pyelitis may exist without involving the kidney substance itself; on the other hand, quite early in some cases, and in the majority of cases after a certain length of time, such involvement does occur. The bacteria usually invade the collecting and the uriniferous tubules, and the inflammation usually starts from these as a centre. Bacteria may penetrate into the lymph spaces and interstitial tissue; we may find scattered throughout the kidney, especially the medulla, although the cortex is also often involved, little areas of suppuration which subsequently coalesce into abscesses of greater size with associated destruction of the surrounding parenchyma. The kidney is usually larger than normal, and is often soft, while if the process is extensive we find abscesses of various size, usually with a fairly thick surrounding sac and in which septa are sometimes seen. Microscopically the affected tubular epithelium shows the usual inflammatory changes, becoming turbid and swollen, and finally disintegrating; fatty changes may occur, and sometimes proliferation takes place. In all cases of ascending pyelonephritis the medullary portion of the kidney is usually affected earlier than the cortical, and to a greater extent.

*Chronic interstitial nephritis* is a quite frequent sequel of pyelitis, the connective-tissue proliferation being seen as much in the medulla as in the cortex, while it is very common to meet many of these pathological conditions in the same case. If suppuration has been present for a long time we may have amyloid degeneration of the kidneys

or of other organs, while in some cases the renal suppuration may be the starting-point of pyemia or septicemia, and in addition we may have extension of the suppuration, either by contiguity or metastasis.

**Hematogenous Infections.**—In these the condition is far more likely to be bilateral than unilateral. We may find a pure pyelitis with practically the picture already described due to metastasis, but in the majority of cases the pyelitis met with in descending infections either arises simultaneously with the infection of the kidney itself, or is a direct sequel to it; in some cases the cortex and pelvis may be involved at the same time, while in others the process is localized first, and often for a considerable time in the kidney substance alone. Areas of hyperemia are followed by suppuration and abscess formation, with masses of bacteria as the causative factor, but unlike the ascending infections the bacteria are more likely to be found in and about the bloodvessels, and the cortex is more likely to be primarily involved. The organ is usually swollen and of a rather mottled appearance, the little abscesses being easily seen through the capsule, which is peculiarly liable to become adherent. Due to the distribution of the bloodvessels we sometimes find that the areas affected become wedge-shaped, with the point directed toward the centre of the organ. When the process becomes chronic, the abscesses, more likely to be found in the cortex, become larger and give a rough appearance to the surface, while the changes in the medulla, although similar in nature, are neither so marked nor distributed with such regularity. It is not uncommon to find bacterial emboli in the bloodvessels.

**Traumatic Infections.**—In these cases we meet, according to the nature of the wound and the character of the invading microorganism, either small, localized foci of inflammation surrounding the hemorrhages due to the injury, or larger abscesses filled with pus, necrotic tissue, bacteria, etc., with marked destruction of the renal tissue; in the most severe types the entire organ may be destroyed, and the suppurative process may involve the renal pelvis, the fibrous and fatty capsules, and the retro-renal fat. The abscesses may burrow along fistulous paths and reach the surface of some neighboring or even far-distant viscus, the frequently associated involvement of the paranephric fat rendering this comparatively easy; the abscesses may rupture directly into the renal pelvis, causing a pyelitis; they may give rise to pyemia or septicemia, or they may set up metastatic inflammations.

**Infections by Contiguity.**—In these the picture is much the same as the preceding one except that the extravasations of blood, the laceration of the kidney substance, and the signs peculiar to injury are lacking.

In any form of renal inflammation, whenever the inflammatory process reaches the surface of the kidney, perinephritis with adhesions between the kidney and its capsule is likely to occur, and from this source the inflammation frequently spreads to the fatty capsule and retrorenal fat.

**Symptoms.**—Many cases of pyogenic infection of the kidney and of its pelvis are devoid of characteristic symptoms, although careful examination, especially of the urine, should throw light on a considerable proportion. The symptoms may be practically wanting or so vague and

indefinite as to be regarded as due to some other cause. It is a good rule that in every case of doubtful etiology, especially if associated with slight pain or sensitiveness in the back or either flank, with vague febrile symptoms, or with constitutional disturbances without definite cause, a careful urine examination should be made with the use of the cystoscope and the ureteral catheter if the urinary findings seem to warrant it. Urinary examinations are peculiarly valuable in infants and children when the symptoms are specially vague and confusing, and in whom the vast majority of cases go unrecognized. In many cases of renal infection the onset is very insidious, while in others the disease may be ushered in by most violent symptoms, severe pain, chills, and high temperature, severe constitutional disturbances, etc. Pyelitis may last for years with practically no symptoms, although, even in those of most chronic course, a careful history usually elicits some suggestive symptoms, such as slight soreness, occasional slight febrile attacks with no apparent cause, and slight urinary abnormalities.

In *acute pyelitis* we may have the usual symptoms of an acute inflammation, fever, chills, constitutional disturbances, etc., while in the *chronic form* acute exacerbations are frequently met with, the symptoms usually resembling those of an acute attack, while between the attacks the symptoms may disappear or become very slight. It is not at all uncommon for the acute cases and the exacerbations of the chronic cases to be regarded as appendicitis, while mild types of the disease are frequently regarded as lumbago.

It is often most difficult to determine when a pyelitis goes over into a pyelonephritis, for even the latter process may last for years without any striking symptoms. Usually, however, involvement of the kidney substance is associated with a marked increase in the severity of the symptoms, the local and especially the constitutional, while if both kidneys are involved very grave symptoms may supervene. In acute pyelitis and pyelonephritis death may occur quickly, or the patient may gradually wear out, the terminal symptoms being sometimes due to general toxemia, at other times to uremia or ammoniemia; the symptoms may suddenly or gradually disappear and a cure take place; the acute may pass into a chronic inflammation, or the condition may be chronic in character from its incipency.

In many cases of *suppurative nephritis* there is a complete absence of symptoms, the manifestations of the primary disease completely overshadowing the renal manifestations, although in the traumatic renal suppurations and those in which the kidney is suddenly affected by metastasis from some local focus, the symptoms, as a rule, are more definite. In abscess sudden rupture may complicate the picture, the symptoms either becoming more or less severe, or even disappearing altogether, according to where the rupture occurs. In *pyonephrosis* the clinical symptoms are most variable according to the etiology. During pregnancy and the puerperium we should always keep in mind the possibility of bladder and renal infections. The presence of leukocytosis sometimes aids in the diagnosis.

The main symptoms of the pyogenic infections of the kidney and its



pelvis are changes in the urine, pain, swelling, and constitutional disturbances, and these will be considered in order.

*Urine.*—In many of the cases the patients themselves have noted urinary symptoms; and pain, increased frequency, and other symptoms may call the patient's attention to the urinary tract, although obviously these symptoms may be entirely referable to the bladder. If ureteral catheterization is done, it is important to watch the rate of flow; normally this is drop by drop, while in cases of pyonephrosis and hydronephrosis and pyoureter and hydroureter the flow is in a steady stream until the ureter or pelvis is emptied, after which the flow is usually very sluggish. When the bladder is infected it is especially important to obtain separate specimens from each kidney.

In *acute pyelitis* the amount of urine is usually diminished, sometimes there is complete anuria due to the severity of the infection, the involvement of both kidneys, or to the stoppage of one ureter and the reflex inhibition of the other kidney. There is usually *increased frequency* of urination, sometimes with pain or burning, even when the bladder is not involved; the specific gravity is usually increased; the reaction is usually acid, but may be neutral or alkaline. In infections with colon and typhoid bacilli it is always acid; in fact, in certain cases its acidity is definitely increased; albumin is usually present, often in moderate amount, due partly to the pus and red-blood cells present, partly to the effect of the fever and toxins. According to most observers, the amount of albumin in uncomplicated pyelitis, whether acute or chronic, can be entirely accounted for by the pus and blood; personal observations, on the other hand, have seemed to show that even when there is no involvement of the kidney the albumin is present in greater amount than can be thus accounted for. Microscopically pus cells, red-blood cells, epithelial cells, mucus, sometimes fibrin, and in all cases numbers of bacteria, sometimes actively motile, are found. In case of hemorrhagic pyelitis, red-blood corpuscles are present in large amount; in a few cases a marked tendency of the pus cells to active pseudopodic movements is seen. If the bacteria cause alkaline decomposition of the urine, the reaction may be ammoniacal and the mucopus thick and ropy, with phosphate and oxalate crystals embedded in it.

In *chronic pyelitis* and *ascending pyelonephritis* the amount of urine is usually increased, although oliguria, and occasionally anuria, are met with in the acute exacerbations; several liters are sometimes passed daily, while in personally observed cases the average amount was 2200 cc.

In *chronic pyelonephritis* the urine may be increased or normal in amount, as in pyelitis, although if both kidneys are involved oliguria is the rule. The specific gravity is usually low, varying with the amount passed, although high in the exacerbations. The color is usually light yellow, although it may be dark red in the exacerbations. The odor is usually slight except in alkaline infections. *Albumin*, consisting of a mixture of serum albumin and nucleo-albumin, is always present; in pyelonephritis the amount is dependent upon the degree of renal involvement, although in many cases it is absolutely impossible to

determine from the albumin, or, in fact, from any other urinary findings, whether we are dealing with a case of pyelitis or pyelonephritis.

It is important to determine the amount of sediment, as by its increase or decrease we can tell something about the course of the disease and the effect of treatment. Immediately after being passed, the urine is usually cloudy, due to bacteria and pus cells, and the sudden disappearance of this cloudiness is very suggestive of stoppage of the ureter.

*Pus cells* are practically always seen and red-blood cells are usually present in small numbers. *Bits of renal tissue*, although very rare, are important in showing kidney involvement. The long-tailed or caudate transitional cells in a tile-like arrangement, which used to be considered diagnostic of pyelitis, are in reality not so, as they are met with in the lower layers of the epithelium of the bladder and ureter. *Bacteria* are always present, often in clumps, sometimes in casts, the latter especially in pyelonephritis while *hyaline*, *granular*, and *epithelial casts* are found in certain cases of pyelonephritis.

In *suppurative nephritis* and *renal abscess* there is usually neither increased frequency nor pain on micturition; the urine may be normal as to its *amount* and *character*. In all cases in which both kidneys are considerably involved, or the kidney which is not affected is not functioning properly, the *quantity* is diminished; the urine may contain *blood* and *pus cells*, *renal epithelial cells*, rarely *bits of renal tissue*, all forms of *casts*, including pus and bacterial casts, if there is much involvement of the kidney tissue near the tubules. The sudden appearance of a large amount of pus is very suggestive of an abscess rupturing into the renal pelvis, and is often accompanied by marked improvement in the symptoms and a lessening in the swelling. In suppurative nephritis and descending pyelonephritis the *bladder* is not so likely to be markedly affected as in the ascending forms. In miliary metastatic abscesses of the kidney secondary to general infections the urine often shows neither pus cells nor red-blood cells, and if present they are usually found in very small numbers.

*Traumatic nephritis* often begins with a transient hematuria followed by anuria. Practically the same urinary findings, barring the initial hematuria and anuria, are seen in *infections by contiguity*. *Pyonephrosis*, if closed, may have normal urine, while if open there is always pyuria, which may be intermittent. In *bacteriuria* the urinary symptoms are usually *nil*; in pure bacteriuria the urine contains no pus cells, but myriads of bacteria, usually colon bacilli.

*Pain*.—Pain, sensitiveness to pressure, or a feeling of pressure or fulness, is often the first symptom that suggests any renal trouble, and if present it is a most valuable sign, although frequently absent, as, for instance, in some cases of pyelitis and pyelonephritis, in metastatic miliary abscesses, in long encapsulated abscesses, and in certain cases of suppurative nephritis and pyonephrosis. In pyelitis and pyelonephritis there may be constant pain or sensitiveness to pressure, or these symptoms may only be present during acute exacerbations; in our series, pain, a feeling of pressure or weight, a girdle sensation, or sensitiveness to pressure was present in more than 75 per cent. of the cases,

although in many instances slight and only elicited by careful questioning. Pain is usually more marked with stone, although in pyelitis alone the pain may be so severe, due to plugging of the ureter, that we may have a typical renal colic, which can only be differentiated from stone by the use of the x-rays, the wax-tipped catheter, or at operation. The pain often radiates downward to the thigh, perineum, or genitalia, or upward to the stomach or shoulder, and it is usually increased on exertion, while pronounced and persistent pain associated with chills and fever is frequently the sign of the formation of a renal abscess consecutive to pyelonephritis. Ureteral pain due to stone, stricture, etc., may be difficult to differentiate from renal pain.

In *pyonephrosis* about half of the patients complain of more or less pain, a considerably larger proportion of pain on pressure, and many have a feeling of fullness or discomfort in the renal region. In *hematogenous suppurative nephritis* and *pyelonephritis* the pain is often rather diffuse at first, later being localized in the renal region, while in the miliary metastatic abscesses met with in the course of various general infections severe pain is rarely present. In infants and young children the presence of colicky pain of doubtful origin, with drawing up of the legs, and screaming if the upright position is assumed, should make us suspicious of cystitis, pyelitis, or pyelonephritis, and should require an immediate urinary examination.

*Swelling.*—Swelling or tumor, if present, is of the utmost value, although its absence does not in the least rule out renal infection. If present at all, it is usually of slight extent, although rarely it may be marked, as in some cases of pyonephrosis, and in renal infections associated with perinephritis and paranephritis; in these latter instances the overlying skin may be markedly edematous. In *acute pyelitis* the swelling is usually slight and often cannot be made out with certainty; in *chronic pyelitis* it is usually not demonstrable except during the acute exacerbations, when it may be quite marked; in *pyelonephritis* swelling may sometimes be made out, especially if there is obstruction to the flow of urine. In *pyonephrosis* the kidney can often be felt, while in *purulent nephritis* with abscess formation the tumor, although rarely of large size, may usually be determined by careful palpation. In cases of *infection by contiguity*, although swelling is often made out, it is difficult to differentiate it from the primary process.

**Constitutional Symptoms.**—These are usually present at some time during the course, although often regarded as due to some other cause. *Pyelitis* and even pyelonephritis may last for years without any apparent constitutional disturbances, especially when the organism is not decidedly virulent, the urinary stasis slight, and the patient naturally vigorous; nevertheless, careful questioning will usually elicit some, if very slight, symptoms, loss of strength, slight digestive disturbances, mild febrile attacks, etc. Encapsulated renal abscess may give no general symptoms, while in many cases of suppurative nephritis in the course of general infections, or due to contiguity from some neighboring focus of inflammation, the constitutional symptoms are in no way different from those of the primary disease. The constitutional effects depend to a great



extent on the amount of absorption, and for that reason are always increased by any condition which obstructs the flow of urine. It has been shown that the poisons produced by certain bacteria have a marked effect upon the nervous system, and also can produce destructive changes in the gastro-intestinal mucous membrane. As these constitutional symptoms are seen in unilateral cases when the urine is normal as regards the amount of urea secreted, etc., they are probably due more to the toxins produced by the infection than to renal insufficiency.

The general symptoms are the usual ones met with in fever and toxemia, although differing markedly in degree according to the virulence of the infection, the resisting power of the patient, the accessory factors present, the amount of urinary stasis, etc. The most common symptoms are chills, fever, and sweats, general physical depression, loss of weight and strength, and digestive disturbances. In *acute pyelitis* there is sometimes in addition diarrhœa, while nausea and vomiting are quite common; the pulse is usually rapid and full. These symptoms last in their severity for only a few days, and then either disappear suddenly or gradually merge into those of the chronic form.

In *chronic pyelitis* the patient may have increased thirst due to the polyuria, appetite is usually diminished, dyspeptic disturbances frequent, and slight fever and diarrhœa are also met with, these symptoms varying markedly in different cases, and possibly being absent altogether; there may be a tendency to profuse sweating, sometimes although not always associated with exacerbations of the disease. Increased pulse tension and enlarged heart are not seen, as a rule, in pure pyelitis, while if the kidney is considerably involved the tension is usually high, and the heart occasionally hypertrophied; there are also sometimes uremic manifestation and changes in the eye-grounds. In the exacerbations the symptoms very closely resemble those of acute pyelitis.

If the kidney is markedly involved in the inflammatory process, loss of weight, coated tongue, marked digestive disturbances, poor powers of resistance, and more or less fever are usually seen, the symptoms resembling to a considerable extent those of small contracted kidney. The more frequent these acute exacerbations of pyelitis and pyelonephritis, the more marked the constitutional symptoms and the more rapid the course of the disease.

Severe general symptoms are the rule in cases of *renal suppuration* secondary to trauma, by contiguity, or from some localized focus of inflammation by metastasis; in some cases a typhoid state with delirium and coma results. True uremia is rare, probably because this type of inflammation is usually unilateral, but in severe cases of alkaline infections, especially if retention is marked, ammoniemia may occur.

In the pyelitis and pyelonephritis of *pregnancy* the symptoms are most capricious, the highest fever and the most severe constitutional effects disappearing in some cases with great suddenness from no apparent cause, or simply due to rest in bed. In most cases, however, such an outcome does not occur, and we have the symptoms of a chronic pyelitis with very frequent exacerbations. In *children* restlessness, pallor, loss of appetite, and depression are often the only signs, and in these, as in

adults, the symptoms of the disease may simulate typhoid fever, tuberculosis, influenza, or gastro-enteritis. The presence of chills and fever in infants is very suggestive of pyelitis.

The *fever* in renal infections is quite variable; in the acute form and in the exacerbation of the chronic and in any conditions producing sudden stoppage of the flow of urine from the diseased organ, it is often very high, sometimes constant, but more often remittent or intermittent, and often associated with chills and profuse sweats. Remittent fever with chills is usually met with in purulent renal inflammations, whether metastatic, traumatic, or by contiguity, while repeated chills with septic temperature are suggestive of an improperly drained abscess. In ascending pyelonephritis fever is rarely absent, while in open pyonephrosis fever and apyrexia are present with about equal frequency.

In all forms of unilateral infection a sudden increase of the constitutional symptoms may be due to infection of the other kidney. Long-standing cases of renal inflammation or cases of great severity may give rise to pyemia or septicemia with their characteristic temperature charts, the patient dying of the pyemia or septicemia itself, from amyloid degeneration, from some intercurrent disease, the rupture of an abscess into the peritoneal cavity, or by hemorrhage from a necrosed vessel.

**Diagnosis.**—In the diagnosis of renal infection many questions suggest themselves: Are we dealing with a disease of the kidney or its pelvis; if so, of what nature? Is one or are both sides affected? If operation is under discussion, is the remaining kidney able to properly perform the renal functions?

Whenever we wish to determine whether the kidney is involved, and if so, to what extent, especially if operation is under consideration, we should make use of the so-called functional tests, which, though not certain, are at least helpful in many cases, the tests, of course, being made with the urines from the two kidneys obtained simultaneously. The functional integrity cannot be determined definitely, it is true, by these tests, as the time is too short, and other factors play a rôle, such as the reflex inhibition of a normal kidney by a diseased organ, but if positive they are of unquestionable value. The most important functional tests are the phenolsulphonephthalein tests, the lactose, potassium iodide, chloride, and possibly diastase determinations, although many other tests described for this purpose have a distinct value.

A cystoscopic examination of the bladder should be made to determine whether cystitis is present, and to carefully inspect the ureteral orifices, for by their appearance we may determine with a high degree of probability in many cases whether or not the renal pelvis or kidney is diseased, and we may also notice the character of the urine flowing from the two openings and determine whether there is any ureteral stoppage; in cases where they are difficult to find we may give indigo, carmine or methylene blue hypodermically, and the flow of colored urine will easily show us the ureteral mouths. In addition, by the use of the ureteral catheter we can determine the presence of stricture, and even measure very accurately its degree; we may measure the capacity of the renal pelvis and determine whether it is distended or not, while by using wax on the

catheter tip we may determine the presence of stone. In infants it is often difficult to obtain the urine for examination, and for this purpose Rotch has suggested allowing the infant to lie on a pad of cotton with rubber underneath it, from which the urine may subsequently be squeezed.

The examination of the kidney itself should be most thorough, as in many cases swelling or sensitiveness to pressure is our only valuable diagnostic sign. By inspection we may occasionally, although very rarely, make out a lumbar swelling, as in certain cases of pyonephrosis and suppurative nephritis, especially if associated with perinephritis and paranephritis, while some claim that the absence of the kidney may be told by change in the contour of the flank. Percussion is rarely of help except in cases in which the enlargement is so marked that it can be made out better by other means; occasionally by inflating the colon through a rectal tube and percussion we may differentiate renal swellings from other tumors. Palpation is the most reliable method, and various procedures should be employed, the patient being made to exhale deeply, the legs somewhat flexed, and the patient sometimes lying on the back, sometimes on the side, occasionally standing; rectal and vaginal examination should be made at the same time, the latter being especially important, since about one-half the ureter may be palpated by this method, and calculus, stricture, thickening, etc., determined. Sometimes, on account of pain, nervousness, very tight muscles, etc., the examination must be made under anesthesia. The *x*-rays may be employed, although they are not of great value except in ureteral and renal calculi, especially those composed of phosphates or oxalates; by the use of a catheter coated with some substance impervious to the *x*-rays the course of the ureter may be determined, while in abscess of the kidney and marked sclerotic changes we may get a deeper shadow than normal, sometimes even simulating stone. The *x*-ray examination of the kidney after injection of collargol through the ureteral catheter is of great value.

Some employ exploratory incision, puncture, or injection, the former being preferable, as puncture may be followed by hemorrhage or persistent fistula; by puncture, pus mixed with urine will determine the nature of the swelling, while after injecting methylene blue into the tumor, if the urine is colored green within a few minutes it shows that the kidney is the source of trouble.

The general symptoms in many cases first suggest the diagnosis. History of pain in the flank, often slight but usually elicited on careful questioning, has been present in most cases at some time during the course of the disease, often regarded by the patient as lumbago, or neuralgia; fever, malaise, sweats, chills, and digestive disturbances are important only in suggesting that some inflammation is present; if no other cause can be found, however, one should always think of pyelitis and renal suppuration, and the urine should be examined at once. In most of the inflammations of the kidney or its pelvis the leukocytes are increased; in mild cases of chronic pyelitis and pyelonephritis, open pyonephrosis, and encapsulated abscess leukocytosis may be absent.

In pyelitis, whether acute or chronic, the diagnosis can almost always be made with certainty by the use of the cystoscope and the ureteral



catheter and by the examination of the urine, except in those rare cases of severe and rapid gangrenous or diphtheritic pyelitis consecutive to severe infection. It must not be forgotten, however, that pyuria may be due to causes outside the urinary tract, such as appendicular abscess, prostatic abscess, or pyosalpinx, rupturing into the bladder, ureter, or renal pelvis.

In *acute pyelitis* the sudden appearance of localized pain associated with chill is an important sign, while in the chronic cases the previous history of the patient, especially constant pain in the flank or slight fever, is very helpful. The presence of casts and an increased amount of albumin points to pyelonephritis, although both of these, especially the former, may be wanting; as a rule, systemic disturbances become more marked with the involvement of the kidney. The result of treatment is of great service in determining whether pyelitis complicates cystitis.

Whether the condition is unilateral or bilateral can always be determined by ureteral catheterization, and usually by a careful history of the case. In pyelitis the functional ability of the kidney is not affected, as a rule, while in pyelonephritis it is usually lessened. Beer has suggested as a differential test the abnormal retention and delayed excretion of methylene blue in the latter affection. In the rare cases of croupous and diphtheritic pyelitis the diagnosis can usually be made from the characteristic findings in the urine, and the same is true if parasites, fragments of stone, or bits of new growth are found in the urine.

In both pyelitis and pyelonephritis *lumbar pain* and *swelling* are most important diagnostic points. The possible *complications* of pyelitis and pyelonephritis are many, such as pyonephrosis, abscess of the kidney, perinephritis, paranephritis, contracted kidney, fistula of the renal pelvis, calculus, ureteritis, and periureteritis. It is quite striking in how many cases, especially those in which acute exacerbations are marked, the diagnosis of appendicitis has been made, frequently followed by operation. Hunner reported four cases in which the two conditions were associated, the appendicitis being primary, the pyelitis or ureteritis secondary and transitory. In the miliary metastatic abscesses met with in the course of general infection a certain diagnosis is usually impossible.

In all cases of *renal suppuration* the diagnostic difficulties are very great, yet in all the finding of the etiological factors, such as trauma, calculus, contiguous focus of inflammation, cystitis, urethral stricture, or prostatic hypertrophy, is helpful. The most important symptoms are the pain and swelling in the renal region and the pyuria. In *renal abscess* the sudden appearance of a large amount of pus in the urine, with a coincident decrease in the size of the tumor and usually in the constitutional symptoms as well, will give us the diagnosis. In encapsulated abscess, closed pyonephrosis, or complete destruction of the kidney the urine may be quite normal. It is not uncommon for the healthy kidney to be regarded as the diseased organ because of its compensatory hypertrophy.

In *purulent nephritis* and *pyelonephritis* the kidney, as a rule, is at first only slightly enlarged, although in the later stages it is usually sufficiently swollen to be made out by palpation; in empyema of the renal pelvis and kidney abscess, the tumor is frequently large and fluctuating, and

practically impossible to differentiate by palpation from hydronephrosis. In cases where renal suppuration is suspected von Bergmann suggests squeezing the kidney with the palpating hands, to see if by this means a large amount of pus is not expressed into the pelvis of the kidney and thence into the urine. In *pyonephrosis* persistent pyuria is the rule, or sometimes pyuria with periods of clear urine between, these latter being associated with increase of the swelling and of the constitutional symptoms. Cathelin reports a case of lumbar abscess from Pott's disease opening into the bladder exactly simulating pyonephrosis.

**Prognosis.**—The course and prognosis vary markedly in different cases, depending upon the character and virulence of the infection, the accessory etiological factors present, the drainage of the kidney, the presence or absence of complications, and the general physical condition. The prognosis, other things being equal, is better in pyelitis than in infections of the kidney substance, in cases in which drainage is good than in those in which urinary stasis is marked, in acid than in alkaline infections.

In *acute pyelitis* the course is usually rapid, the acute stage rarely lasting more than a few days; in very rare cases death may occur quickly, due to anuria with uremia, although, as a rule, either cure takes place or the condition becomes chronic. If proper treatment is inaugurated cure is usual where the cause is transient or easily removed, as in the case of irritating drugs, while in the case of the acute infectious diseases, cystitis and inflammations of the kidney substance, the prognosis of the secondary pyelitis depends largely on the character and duration of the primary disease and the possibility of carrying out satisfactory therapeutic measures.

The course of *chronic pyelitis* is variable. It may be present for many years, especially if the causal factors remain; the symptoms may be very slight, with no appreciable impairment of the general health, this being most likely to occur in infections with the colon bacillus. On the other hand, the majority do not run so mild a course, while complete recovery is very unusual. This is especially so when the accessory etiological factors persist, as hypertrophy of the prostate, vesical paralysis, etc. The course is subject to very marked variations as regards the symptoms, and marked constitutional disturbances are not infrequent. In the writer's experience stone is always present in chronic infections due to bacteria which have the power to decompose urea; in 5 such cases, 3 due to *Bacillus proteus vulgaris*, 2 to a white staphylococcus, a phosphatic stone was found in each; in one case of infection with the colon bacillus a stone of uric acid and urates was found.

*Simple pyelitis* may go on for years without renal involvement, but if such involvement occurs the usual sequels of destructive renal changes occur; if, however, the kidney is only slightly affected, the clinical picture in many cases is hardly appreciably changed. In all cases the prognosis is worse with alkaline infections, because of the greater destruction of the mucous membrane, the possibility of ammoniemia, and the probability of stone.

In the pyelitis of *pregnancy* spontaneous cure may occur, sometimes

simply due to rest in bed, at other times after delivery, but in many cases a chronic pyelitis, sometimes associated with salpingitis, or a bacteriuria remains. In *children* spontaneous recovery is quite common.

In *suppurative nephritis* there are often no definite symptoms, while in other cases, if present, they are lost in those of the primary disease; death occurs in practically all these cases due to the almost universally fatal termination of the general septicemia, and to the fact that it is in the most severe types that the kidney is likely to be involved. In *traumatic suppurative nephritis* the prognosis is fair if the pus can freely discharge into the renal pelvis, while if the discharge be external the symptoms may be mild, although here there is a great tendency to the formation of burrowing abscesses, retention of pus, etc., which finally end the patient's life. Practically the same course is followed in renal suppuration by extension, but the prognosis is much more serious.

*Renal abscess*, whatever be the cause, may last for a long period of time with practically no symptoms; sooner or later, however, in the majority of cases, rupture takes place into the renal pelvis with the development of pyelonephritis, pyonephrosis, or empyema; perinephritis and paranephric abscess are frequent accompaniments.

Cases of *pyonephrosis*, if unilateral, may last for years, although oftener the constitutional disturbances are marked and the course more rapid; the prognosis is much graver if both sides are affected, or if the second kidney undergoes degenerative changes due to the toxemia. Cure may occur in pyonephrosis and in large renal abscess by the complete destruction of the kidney, but this is very exceptional.

In the renal suppurations the course may be, on the one hand, very mild, sometimes even with no definite symptoms, and, on the other hand, may be associated with symptoms of the gravest kind; in all cases the prognosis depends largely upon the etiological factors; the much more satisfactory treatment of prostatic hypertrophy and chronic cystitis within recent years has unquestionably improved the prognosis. Pure bacteriuria may cause renal inflammation if the local or general resistance is lowered. Küster mentions four favorable factors in the prognosis, the possibility of an early correction of the urinary stasis, youth, a strong constitution, and a unilateral lesion.

**Treatment.—Prophylaxis.**—To properly carry out prophylactic measures it is essential that we should recognize the usual etiological factors and remove them if possible. These may be roughly divided into two groups: first, those that lower the resistance of the kidney by producing retention of urine, trauma, congestion, etc., and second, those that furnish the infection either by direct extension, as in the case of contiguous foci of inflammation, or by metastasis, as in the case of distant areas of inflammation, or by an ascending urogenous infection. It is, therefore, important to avoid all irritating drugs; to adopt the greatest care and most rigid technique in the use of instruments; to avoid introducing infection or producing trauma; to treat with care and promptness all cases of cystitis and gonorrhoea; to remove if possible all causes of urinary stasis, as by operation in urethral stricture, phimosis, and hypertrophied prostate, and hydraulic dilatation in the case of contracted bladder;



to remove such causes of irritation as stone, foreign bodies, etc.; to use some form of urinary antiseptic, such as hexamethylenamine after operations, especially if on the kidney, or if the patient has to be frequently catheterized, after severe labors, during typhoid fever, in bacteriuria, etc.; to give large quantities of water under these conditions, either by mouth or by rectum, as by the latter method most of the fluid is eliminated by the kidney within two or three hours. It is advisable to give plenty of water in severe febrile diseases, in pregnancy, and in the latter case to insist upon a certain amount of rest in the prone or knee-breast position; and, in addition, in this as in all other cases, to build up the patient's health, avoiding above all things constipation; in children and infants, especially girls, to give plenty of water, and to insist on great cleanliness of the genitals, always washing from the front backward. If catheterization has to be done for any purpose one should be most careful in the technique and the patients should drink considerable water beforehand. In the traumatic cases prophylaxis is most important, asepsis and antisepsis in the treatment of the wound, rest, appropriate diet, plenty of fluid, and some of the urinary antiseptics.

In the treatment of inflammations of the kidney and its pelvis it is essential that the causal factor should be recognized and removed if possible. In all cases the resisting power of the patient is to be increased by careful attention to the general health, correcting any disorders, especially digestive disturbances, constipation and anemia.

In acute pyelitis and pyelonephritis the removal of the cause is sometimes sufficient to produce a rapid cure. The patient should be kept in bed at an equable temperature, it being specially important to avoid chilling; the diet should be simple, a milk or buttermilk diet being often best; all irritating drugs, highly seasoned food, and beverages containing alcohol should be avoided; an ice-bag may be applied, although a hot-water bag or hot, moist applications are generally more grateful to the patient; warm baths or sweats sometimes give much relief; if the fever is high, phenacetin, quinine, or some other such remedy is indicated, these being more effective than cold sponges. If the pain is very severe, dry or wet cups or very hot compresses may be tried, although usually recourse will have to be had to morphine or opium, either by mouth, hypodermically, or by suppository. The bowels should be kept freely open and the patient made to take much water, while if the stomach is upset, salt solution or sterile water may be given by enema or, in very severe cases, by infusion.

The urinary antiseptics are practically always indicated—hexamethylenamine (urotropin), salol, etc., in doses of from 5 to 10 grains three or four times daily, with the usual reduction in dose in the case of infants and children; these drugs are peculiarly valuable in acute infections, if one can judge from clinical observations. Sleeplessness and nervousness may be helped by the bromides, trional, or veronal. If the urine is acid, bicarbonate or citrate of soda or potash may be given; if alkaline, boric, benzoic, or camphoric acid, as it is probable that the growth of the bacteria is inhibited in a medium of different reaction from what it

is accustomed to. If the severe symptoms persist, nephrotomy may be necessary.

In chronic pyelitis and pyelonephritis, if the cause has been determined, it must be treated promptly. The resisting powers of the patient are to be increased by the usual procedures. The medicinal treatment consists in the administration of urinary antiseptics, or of the astringents, lime-water, lead acetate, gallic or tannic acid, etc., or of such drugs as uva ursi, the balsams of copaiba and Peru, etc. Of these drugs, hexamethylenamine or its derivatives may be taken for a long period of time without doing apparent harm, although some claim that it should not be used in gouty or lithemic subjects, or when uratic calculus is present. In all cases of chronic pyelitis or pyelonephritis some of the urinary antiseptics should be tried, but the drugs of the other groups are but little used, as they do little if any good in the majority of cases, besides deranging digestion; in persistent, intractable cases, where the other means have been unsuccessful, they may be tried, however. Obviously in the case of the antiseptics the effect on the deeper tissues is much less than on the pelvic mucous membrane, and they are, therefore, of less value when the kidney itself becomes involved in the infectious process. It is wise to change the reaction of the urine by giving alkalis or acids by the mouth with water in large amounts; if the kidney itself is much involved, however, one should avoid giving too large amounts. In cases of ammoniacal decomposition chlorate of potash, boric, benzoic, or camphoric acids may be given.

In the pyelitis and pyelonephritis of pregnancy artificial labor must be induced, or a nephrotomy or even nephrectomy performed if the symptoms are very severe and very persistent and do not yield to the usual treatment. Dilatation of the bladder sometimes gives marked relief in this as in other forms of renal infection. Sometimes the patients are much benefited by treatment at one of the alkaline springs. The acute exacerbations are to be treated in the same way as acute pyelitis.

Chronic pyelitis has been treated by Kelly, Casper, and others by instillation into or irrigation of the renal pelvis through the ureteral catheter, the results in most cases being most encouraging, especially in infections with the colon bacillus or the gonococcus. Solutions of boric acid or of nitrate of silver (1 to 2000 to 1 to 1000) or other antiseptics may be used every few days as an irrigation, or 5 cc. of a 1 to 2 per cent. solution of silver nitrate instilled; by these means a number of cures have been reported, Casper obtaining a cure in 12 stubborn cases, 9 due to the gonococcus, 3 to the colon bacillus. If we have pyelonephritis or if the pyelitis is associated with tuberculosis or calculus, this treatment can only be palliative and should not be employed. The use of autogenous vaccines is indicated, although in the main the results of these have been discouraging. The author has employed this method in a number of cases of infection with the colon and proteus bacilli, but usually with very disappointing results.

In certain cases *operative* treatment may be necessary, either nephrotomy, nephrectomy, pyelotomy, or resection. In all cases, however, it is essential that the presence and the functional ability of the other

kidney be determined before operation is performed. In double pyelonephritis, if the condition warrants it, operation may be performed first on one kidney, and at a later time on the other, the kidney being opened, washed out, and drained. If the pyelonephritis is associated with abscess formation, free opening and drainage or nephrectomy is indicated according to the extent of the process. Some brilliant cures in the case of unilateral pyelitis and pyelonephritis have been reported after nephrotomy.

In suppurative traumatic nephritis, and that by extension from neighboring infections or by metastasis from a distant focus of inflammation, the two main indications are to remove the cause if possible or to lessen its manifestations, and to make an early and free outlet for the pus. If an abscess arises after trauma, the wound should be widened, washed out, and drained, while in only very severe cases is resection, nephrectomy, or nephrotomy necessary. In cases of pyelonephritis, whether due to ascending or descending infection, we should first try the measures already described, diet, rest, the use of alkaline waters, urinary antiseptics, etc.; in many cases great relief is obtained by these methods, but if marked suppuration occurs operative treatment is necessary. In suppurative nephritis and pyelonephritis with the formation of abscesses, operative treatment should be employed as early as possible, but not until the presence and the functional ability of the other kidney has been determined, even if an exploratory nephrotomy is necessary, although usually the results obtained by ureteral catheterization are sufficient.

The possible operations are pyelotomy, pyelostomy, nephrotomy, nephrostomy, resection of the kidney, and nephrectomy. If the ureter is narrowed or closed, nephrostomy or pyelostomy should be done and an attempt made to dilate the constricted portions of the ureter from above; persistent fistula is a frequent sequel to these operations. On account of the well-known regenerative powers of the kidney, resection or nephrotomy should be the operation of choice if only a comparatively small and localized portion of the kidney is markedly affected. When nephrectomy is done, as much as possible of the diseased ureter should be removed at the same time, although this is not so important as in the case of tuberculous infections. It is always justifiable to perform these smaller operations first, and later a secondary nephrectomy if necessary. A primary nephrectomy should practically never be done if the second kidney is diseased for a nephrotomy with drainage of the more diseased organ will often give an opportunity for the patient's general health to be improved, so that the secondary nephrectomy, if found to be necessary, will offer a better prognosis. In pyonephrosis, nephrotomy or nephrectomy is usually necessary, although irrigation of the renal pelvis may be very beneficial in a small proportion of the cases.

Rovsing concludes that death from insufficiency of the other kidney should never occur if the modern methods of diagnosis are carefully and intelligently employed; if the urine is free from pus, albumin, and bacteria, the kidney may be regarded as normal, while the presence of pus and bacteria usually contra-indicates operation on the other kidney. Albumin



without pus and blood, according to Rovsing, is often simply a sign of toxemia, and is a strong indication for operation.

As to the results of the operative treatment of suppurative nephritis and pyelonephritis, Küster gives the following figures: In 100 nephrotomies, 27 were cured, 56 were unhealed, and in 23 of these a secondary nephrectomy was done, 17 died; 2 cases of resection each gave favorable results; in 143 lumbar nephrectomies there were 24 deaths, and in 7 transperitoneal nephrectomies, 4 deaths.

#### **PERINEPHRITIS—PARANEPHRITIS—EPINEPHRITIS—PARANEPHRIC ABSCESS—PERINEPHRIC ABSCESS**

The words perinephritis, paranephritis, and epinephritis have been used loosely to signify indiscriminately inflammation of the perirenal tissues, while Rayer, who first differentiated inflammation of the perirenal tissue from that of the kidney, first made use of the term perinephric abscess. It is better to be more explicit, however, and to define perinephritis as inflammation of the fibrous capsule immediately surrounding the kidney; epinephritis, inflammation of the fatty capsule, and paranephritis, of the retroperitoneal fat. Of the three forms of epinephritis described by Israel (exclusive of the tuberculous, the syphilitic and actinomycotic), which he calls fibrosclerotic, lipomatous, and phlegmonous, the first two are so extremely rare, and the last so frequently gives rise to paranephritis that it is wise to consider epinephritis and paranephritis together under the one term, paranephritis.

*Perinephritis*, although very rarely an independent disease, and in the vast majority of instances secondary to various inflammations of the kidney or of the perirenal fat, is of great interest because, due to the dense adhesions formed and the inability of the capsule to be easily moved over the kidney surface, symptoms almost exactly like those of renal colic may be produced.

*Paranephritis*, and we are now using the term to include inflammation both of the fatty capsule and of the retroperitoneal fat behind the kidneys, while much less common, is of far greater importance, as it gives rise to paranephric or perinephric abscess. Perinephritis and paranephritis often occur together, although the process almost always begins either in the fibrous capsule, the fatty capsule, or the retrorenal fat, extending then to the others. As to the frequency of the condition Küster has collected 230 cases of paranephritis, finding that it is twice as frequent in men as in women, equally frequent on either side, and that most cases occur between the ages of twenty and forty years; only 4 or 5 cases have been reported in which both sides were affected. Nieven, in a series of 144 cases, found 97 in man, 47 in women, and in a series of 166 cases, 26 in children up to thirteen years, the youngest being five weeks old; 5 cases were found between the ages of sixty and seventy years, while the greatest number were met with in the fourth decade; in 136 cases the right side was affected 76 times and the left side 60 times.

**Etiology.**—Paranephritis may be either primary or secondary, the former usually developing from penetrating wounds and injuries of the

kidney and perirenal tissues, the latter usually arising from metastasis or extension of inflammation from neighboring organs or tissues. Among the causes of the so-called primary form may be mentioned penetrating wounds and various contusions, blows in the region of the kidney, lifting heavy weights, sudden strain, hard riding, in fact, any condition which may cause a slight tear with associated hemorrhage into the perirenal tissues, this acting as a nidus for infection if any bacteria are brought there by the blood-stream. Foreign bodies from the intestine have been the cause in a few cases, while in some cases exposure to cold is the only causal factor that can be made out.

The so-called secondary form arises either by metastasis, the infection being carried by blood or lymph current or by direct extension from some neighboring focus of inflammation or suppuration, as in puerperal infections. Küster believes that the cases met with in contagious diseases are not due to the primary disease, but to a secondary infection with pyogenic bacteria. In all these cases it is not known whether the kidney or its capsule is affected first.

The most common cause of paranephritis by direct extension is purulent inflammation of the kidney itself, while among other causes may be mentioned various suppurations in the pelvic cavity, such as parametritis and rectal abscess, appendicular abscess, psoas abscess, etc. Operations on the bladder and the genitals are followed occasionally by paranephritis. Of course, bacteria are always the immediate cause of the inflammation, and among those found in paranephric abscess may be mentioned staphylococci, streptococci, the pneumococcus, and colon, typhoid, tubercle, and influenza bacilli.

**Pathology.**—We are rarely able to study the early stages of paranephritis, but probably there is no difference between this and inflammations elsewhere, except that in the traumatic cases the inflammation is probably preceded by small hemorrhages into the fat. When seen at operation or autopsy we usually find the fatty capsule and retroperitoneal fat converted either into one large abscess, or into several smaller abscesses separated from each other by more or less necrotic fat and connective tissue. The picture is similar to that met with in other abscesses, and a distinct pyogenic membrane is often seen if the condition has been present for a considerable length of time. The retroperitoneal fatty tissue is especially likely to be the seat of the pus; the upper and lower poles are frequently affected, while that portion anterior to the kidney is rarely involved, although if it should be we will find a circumscribed local peritonitis, occasionally a general peritonitis due to perforation. An abscess in the true fatty capsule tends to burrow along the ureter toward the pelvis, while one of the retrorenal fat points more toward the inferior or superior lumbar triangle. The pus is sometimes odorless, sometimes has a fecal odor, due probably to proximity to the large intestine, or it is putrid if gangrene has occurred. The kidney may undergo various inflammatory changes, although, as a rule, the fibrous capsule protects it for a long time. We may find amyloid degeneration or pleurisy with effusion on the affected side if the condition has lasted long.

**Symptoms.**—In the majority of cases, due to the fact that the lesion is so deep seated and that the symptoms are usually masked in the early stage at least by the primary disease, an early diagnosis is difficult to make. In certain cases of insidious infection of different parts of the body, however, the first symptoms may be referred to the paranephric region, and only later the fact made out that the primary focus of infection is elsewhere. If the condition follows injury, the symptoms are more likely to be referred definitely to the paranephric region, pain usually being the first symptom. In the secondary cases as the disease progresses the true nature of the lesion usually can be made out. The three important symptoms are pain, lumbar swelling, and fever. The *pain* is usually the first symptom, often extremely severe, localized in the lumbar region, and increased by every movement, and by direct pressure. The *fever* may be remittent or intermittent, the usual condition, or it may be continuous, high or low, or absent altogether. The *local swelling* usually first appears in the back, and by palpation a smooth, elastic, usually fluctuating mass, generally fixed, and not affected by the respiratory movements, can be made out. It is, as a rule, more diffuse, not so well defined, and not so distinctly limited as a renal tumor. The skin is often oedematous if it points outward, while it may also become reddened and swollen when the inflammation gets near the surface.

The urine, as a rule, is normal except in those cases in which the primary disease is one of the kidney or its pelvis. The general symptoms are those usually found in abscesses. If rupture occurs the size of the tumor may diminish and the pain disappear. As to the localization of the seat of the abscess, Maas, Roberts, and others have mentioned special symptoms; difficult breathing with persistent vomiting and pleuritic pain would thus suggest suprarenal abscess; constipation and flexion of the hip, infrarenal; pain on pressure and early lumbar tumor, retrorenal, while there are no typical symptoms, except possibly those of a local peritonitis, to suggest an abscess in front of the kidney.

**Course.**—The primary and secondary forms of the disease differ markedly as to course and duration, the former usually beginning suddenly with a fairly rapid course, the latter being slow and insidious. In every case the course is dependent upon the position of the abscess, the direction of its burrowing, the character of the primary disease, and the associated complications. The pus may burrow along the psoas muscle to Poupart's ligament, along the ureter into the bladder, or may rupture into the intestine, especially the cecum or colon, ureter, peritoneal and pleural cavities, and in many cases fistulae occur, which, although persisting a long time, usually spontaneously heal. In rare instances the kidney may undergo gangrene due to thrombosis of its vessels, or an atrophic nephritis may be caused by the contraction of the inflamed perinephric tissue. Rosenberger collected 26 cases of perforation: 6 into the intestine, with 2 deaths; 13 into the pleural cavity and lungs, with 8 deaths, and 3 into the peritoneal cavity, with 3 deaths. Even in favorable cases the duration of the disease is several weeks, while in the unfavorable cases, especially those secondary to causes which persist, the condition may last for years, and death may



finally supervene, either by pyemia or septicemia, by gradually wearing out the patient, or by the development of amyloid degeneration.

**Diagnosis.**—Early diagnosis is always difficult because, in the first place, the most important symptom, tumor, cannot be made out early, and in the second place, the symptoms are usually masked by those of the primary disease; specially difficult are the rare cases without fever. Pain, the first symptom, is frequently regarded as due to lumbago, although in the latter disease this is usually bilateral, less likely to be associated with leukocytosis, and is usually not so definitely localized in the soft parts. The general symptoms often suggest one of the acute infectious diseases. It is always well to remember, as Israel insists, the fourfold character of the symptoms in paranephritis, the general toxemia, localized symptoms, such as pain, those due to the extension of the abscess, and those due to acute metastatic involvement of the kidney, such as vomiting and changes in the urine. Even with pain, fever, and localized swelling the condition must be differentiated from all other causes of similar signs and symptoms in the kidney itself; but here the examination of the urine, and the fact that in paranephritis the swelling is less distinctly limited, is usually retrorenal, and is affected little by the respiratory movements, should be helpful. The urine is normal, unless the disease is consecutive to a pyelitis or pyelonephritis. In distinguishing other abscesses in this region, extensive appendicular, psoas, and parametric abscesses and abscess of the subcutaneous tissue, great difficulties may be experienced, although usually a careful examination with a consideration of the etiology and course will make the diagnosis certain. In doubtful cases puncture is justifiable, and if there is much admixture of fat with the pus we are probably dealing with a paranephric abscess. In a few cases the x-ray may be helpful.

**Prognosis.**—This depends on the conditions surrounding the special case, being most favorable in those cases pointing outward, or where surgical interference is early, and thus, as a rule, good in the primary type of the disease, and least so when the pus is difficult to recognize or to reach, when the primary disease is intractable, or when complications occur. The prognosis is peculiarly dependent upon the skill of the physician in making an early diagnosis. In Küster's series of 230 cases of paranephritis there was a complete cure in 145, a persistent fistula in 6, while death occurred in 79, that is, 34 per cent. of the cases.

**Treatment.**—Before the diagnosis can be made with certainty some of the symptoms, notably pain and fever, require treatment. We may use the Paquelin cautery, hot and cold applications, cupping, various drugs, aspirin, phenacetin, the salicylates, etc.; with very intense pain morphine must be given hypodermically. It is highly improbable that any of these measures have the least effect on influencing the disease. As soon as the diagnosis can be made with certainty there is but one course to pursue; the abscess must be freely opened and drained, its cavity explored so that all pockets of pus can be broken down, while if there is any question of the kidney being also involved it must be investigated by palpation, or by incision, and nephrotomy or nephrectomy be done if necessary.

## URETERITIS—PERIURETERITIS

With few exceptions inflammation of the ureter occurs only in association with an ascending infection from the bladder or a descending infection from the kidney and its pelvis, and for that reason as independent affections ureteritis and periureteritis are of small moment, their symptoms being practically included in those of the primary disease. Pyogenic inflammations of the kidney and its pelvis, except those of a transitory nature, practically always involve the ureter to a certain extent, although often only the upper portion is affected, while ureteritis consecutive to bladder inflammations is less common. As to its *etiology*, the causative factors are the same bacteria which give rise to pyelitis on the one hand and cystitis on the other. Israel, White, Stein, and Viertel have each reported cases of primary ureteritis, the symptoms being those of a nephralgia with hematuria, while a chronic proliferating ureteritis of doubtful etiology has been described. Tuberculous ureteritis is especially important, for in most cases of renal tuberculosis the ureter becomes involved, often along its whole course, so that the nature of the disease may be revealed by a cystoscopic examination; whether tuberculosis of the bladder can infect the ureter and subsequently the renal pelvis by direct extension is still a matter of discussion, although certain findings are difficult to explain otherwise. Among other etiological factors of importance may be mentioned various new-growths and areas of inflammation in the neighboring tissues, pyosalpinx, appendicular abscess, etc., and especially ureteral calculus, for whether primary or secondary, the ureteral wall may be so injured that inflammatory changes will be easily set up if pyogenic bacteria are present. Those cases of ureteritis and periureteritis due to extension of inflammation from some nearby focus are interesting, as when such infection occurs from the inflamed appendix, and such cases are especially important because of the possibility of overlooking the primary disease.

The ureter is usually markedly thickened, especially in tuberculous ureteritis, and if the lower portion is affected the vesical orifice is swollen, œdematous, or ulcerated. Frequently the periureteral tissues are involved, and we have a periureteritis, or rarely a periureteral abscess, which may be edematous, infiltrated, or ulcerated, while it is very common to meet constriction of the lumen, sometimes complete closure, kinking of the ureter in its course, or dilatation, the last being specially likely to occur above a stricture or an impacted stone, and sometimes leading to hydronephrosis, pyonephrosis, or pyoureter.

**Symptoms.**—The symptoms of ureteritis and periureteritis ordinarily met with in association with kidney or bladder infections are of no special significance, but it must not be forgotten that stricture of the ureter may produce symptoms simulating very closely those of nephrolithiasis or nephralgia. The *course* of ureteritis is practically the same as that of the primary disease, and yet it undoubtedly plays an important rôle in the development of complications. In diseased conditions a reflux of fluid from the bladder can undoubtedly occur, and thus the

ureter has a very important intermediary rôle in the development of pyelitis and pyelonephritis consecutive to cystitis.

**Diagnosis.**—This may be safely made if the physical signs, especially the urinary findings, show the presence of pyelitis or pyelonephritis, while in cases of cystitis which do not yield satisfactorily to treatment, a ureteritis and probably also a pyelitis may be suspected. In such cases a cystoscopic examination of the ureteral orifices with the use of the ureteral catheter is of paramount importance, while in the case of women the thickened ureter met with in ureteritis, especially in the tuberculous form, may be palpated through the vagina. Ureteral strictures and kinks may be made out easily by ureteral catheterization, Kelly even measuring the tightness of the stricture by a careful estimation of the pull on the catheter or the resistance to its withdrawal, while if the *x*-rays are used in conjunction with a catheter impervious to these rays the course of the ureter may be accurately determined. In cases in which stone is suspected as a causative factor, by means of the wax-tipped catheter or the *x*-rays its position may be determined, especially if the stone is composed of phosphates, oxalates, or carbonates. In the case of the *x*-rays we must be careful not to mistake a phlebolith for such a stone. It is possible if there is infection only of the lower portion of the ureter to find pus in the urine if the ureteral catheter is inserted but a short distance, while if it is pushed beyond the infected area the urine is clear.

**Treatment.**—This is closely connected with that of the primary disease. It is well to remember the frequency with which the ureter is involved in infections of the kidney and its pelvis, for many failures have resulted from a lack of appreciation of this fact, especially in cases of tuberculous infection. It is therefore essential, if nephrectomy is done, that if possible the diseased portion of the ureter be removed at the same time, even if this requires a complete ureterectomy with removal of a portion of the bladder wall; this is peculiarly so in cases of tuberculous nephritis and pyelitis. Periureteral abscess must be treated by incision and drainage, either externally or, in the case of women, by the vagina. If stone is associated with ureteritis, ureterotomy, ureteronephrotomy, or ureteronephrectomy must be done according to the size and position of the stone and the condition of the kidney. In such cases, as well as in stricture of the ureter due to other causes, resection and anastomosis have been done, although in most cases a fistula remains. Occasionally operative treatment can be better carried out through the bladder, the perineum, or the vagina.



## CHAPTER XVIII

### TUBERCULOSIS OF THE KIDNEY

BY THOMAS R. BROWN, M.D.

TUBERCULOSIS of the kidney is met with in two distinct clinical forms: First, as part of a general miliary tuberculosis, both kidneys usually being involved, and the renal disease being usually of comparatively slight significance, because it is but a part of the general infection; and second, the so-called primary renal tuberculosis, in which the disease is confined mainly to the urinary apparatus. Obviously the term primary is used in a clinical rather than in an etiological sense, as it is questionable if there are any cases of primary renal tuberculosis in the true sense of the word, and Krönlein, therefore, suggests the terms combined and solitary. This clinical differentiation, however, is of the utmost importance, as our attitude toward the two is absolutely different. In one there is practically nothing to be done, and the diagnosis, made with great difficulty, if at all, helps little, if any, in our subsequent treatment; while in the other form the health and life of the patient depend upon a proper appreciation of the condition and an early diagnosis, for in this form prompt and proper treatment is followed by brilliant results in a large proportion of cases. It is, therefore, this second form of the disease, primary, primitive, or solitary tuberculosis of the kidney, or chronic localized tuberculosis, to which most attention should be directed.

For many years the character of the disease was entirely misunderstood, and the reasons for this were manifold; in the first place, the disease as seen by the pathologists was usually advanced, bilateral and incurable, and generally associated with considerable involvement of other organs; in the second place, for a long time tuberculosis was supposed to be peculiarly liable to affect the genito-urinary tract in its entirety, and hence the misleading phrase urogenital tuberculosis; while in the third place it was thought that in the great majority of cases the kidney was infected from the bladder by an ascending or urogenous route—all these views obviously suggesting the inadvisability of local treatment. These views were entirely incorrect, for the so-called primary form of the disease is in its incipency almost always unilateral. It is only infrequently associated with genital tuberculosis, and even then there is rarely any direct connection between the two; it is usually due to a hematogenous or descending infection, the kidney being affected first. In its early stages at least the primary source of infection, a tuberculous gland, etc., is often of slight moment, and the prime requisite for successful treatment is its early recognition.

Treatment must be mainly surgical, and yet the success of the surgeon is absolutely dependent upon the acuteness and skill of the physician

in making an early diagnosis. Exactly why the tuberculous process should engraft itself upon one system, and remain confined to that system for a considerable period of time, we do not know; but the urinary system is no exception to this rule, and it is surprising for how long a time tuberculosis of the kidney alone, or of the kidney, ureter, and bladder, may persist without any active manifestations of the disease elsewhere.

**Etiology.**—The only question under discussion is that relating to the origin of the primary form, for in the case of acute miliary tuberculosis and the involvement of the kidney in the terminal stages of tuberculosis elsewhere the infection is hematogenous, the renal disease being but part of a general tuberculosis. The etiology in that form in which the involvement of the urinary system dominates the picture is of the utmost importance. There are three possible ways in which the kidney may become infected by tubercle bacilli: (1) The hematogenous or descending route; (2) the ascending or urogenous; and (3) infection by continuity from some adjoining focus. The last of these, though interesting, is extremely rare and of slight clinical importance. Cases have been described of extension from spinal caries, tuberculous empyema, tuberculosis of the adrenals, of the intestines, and of the peritoneum. In this connection the suggestion that renal involvement following vesical tuberculosis may be by continuity through the course of the ureter is of interest.

The relative importance of the ascending and descending modes of infection has been the subject of much discussion. Guyon and many of the older clinicians taught that hematogenous infection was extremely rare. The work of Baumgarten, Albarran, Israel, and others has shown how erroneous these older views were, and has given us the proper conception of the pathogenesis of primary renal tuberculosis. Baumgarten by animal experiments showed that the infection in tuberculosis travels with the current, not against it, in other words, from the kidney to the bladder; that in the genital tract the epididymis is the favorite seat of primary infection, but that the involvement of the two systems is quite independent of each other, although the bladder may be infected in either case, very rarely, however, from the genital system. Walker inoculated the bladders of several hundred rabbits with bovine tubercle bacilli, and his experiments show that the kidney is practically never affected by an ascending pyelitis or pyelonephritis; he found in his entire series only one case which could be ascribed to this mode of infection, and showed that the ureter is often affected, although generally showing but simple dilatation, and that the urinary organs were affected very rarely from the genitalia. Israel reported four cases of tuberculosis of the epididymis and the kidney on the same side without involvement of the bladder, showing that tuberculosis of the kidney and genital apparatus may occur together without extension from one to the other, both in all probability being infections of hematogenous origin. To quote from the same author: "A large number of cases of tuberculosis of the urinary apparatus show that the kidney is either the only or the first affected portion," and he bases these conclusions on the following facts: postmortem tuberculosis of the kidney with no other disease of the genito-urinary apparatus; lasting health of the patient after removal

of the tuberculous kidney; the localization of the tuberculous changes in the bladder about the ureteral orifices; and the presence of fresh early tuberculosis limited to these same localities.

As a rule, in experimental hematogenous infections the bacteria gather mostly in the glomerular capillaries, going thence into the surrounding tissues, the smaller bloodvessels, or through Bowman's capsule into the uriniferous tubules, as Walker, Bubay, and others have shown. The extreme rarity of primary tuberculosis of the bladder in another argument in favor of the hematogenous origin of renal tuberculosis, Kelly having seen but one such case. It must also not be forgotten that if the bladder were the seat of the disease the kidney might be infected from this either by direct extension of the process up the ureter—a less likely mode of infection—or by the blood-stream as from any other tuberculous focus; in this latter case this may be either by the general circulation, the vesico-utero-ovariorrenal anastomosis or by the bloodvessels of the ureter, and in the later stages of the disease the infection of the second kidney is probably either by this route, or from some other tuberculous focus. Many authors absolutely deny the possibility of a urogenous infection of the kidney, but Albarran, Walker, Küster, Wildbolz, Rovsing, and Casper have proved its possibility in a very small percentage of cases.

The primary source of the infection often cannot be determined, probably being some infected mediastinal, bronchial, or mesenteric gland, or some slight bone lesion, while in other cases an apical tuberculosis, a cheesy gland, or a tuberculous sinus may be found. Garceau's figures seem to show that the lungs or the intestinal tract are the most common source of infection in renal tuberculosis. Kelynnack found the lungs affected in 70 per cent. of his cases of renal tuberculosis, while Flick and Walsh from studies made at the Phipps Institute consider it probable that more than half of the patients suffering from pulmonary tuberculosis eventually have tuberculosis of the kidney, and that tubercle bacilli are excreted in the urine in all cases of active tuberculosis.

**Accessory Etiological Factors.**—In most cases it is impossible to find out any special predisposing factors, although it is highly probable that at the time of its infection the kidney suffered some lowering of its resistance, possibly due to some transitory cause. Among the predisposing causes which may be mentioned are an inherited tendency to tuberculosis, chronic pyelitis, cystitis and urethritis, gonorrhoea, congenital deformities, especially lobulated kidney, pregnancy, which may produce urinary stasis and renal congestion, floating kidney, cold—frequently mentioned, but extremely doubtful—calculus, hypernephroma, hydronephrosis, trauma, and any conditions which may produce urinary stasis, such as hypertrophy of the prostate, phimosis, and stricture. In floating kidney the lowered resistance is probably due to congestion. Küster found this as the apparent cause in 18 of his 403 cases, and this may be the reason why women are affected more than men, and the right kidney more than the left.

**Age.**—As regards primary tuberculosis of the kidney practically all authors agree that the commonest age is between twenty and forty years. In Roberts' series 4 cases were met with in the first decade, 5



in the second, 6 in the third, 9 in the fourth, 9 in the fifth, and 2 in the sixth; in Krönlein's 51 cases, 7 were between seventeen and twenty, 23 in the third decade, 14 in the fourth, 6 in the fifth, and 1 in the sixth. In Morris' 12 cases, 7 were older than thirty years, 5 between eleven and thirty years. Cases of primary tuberculosis have been met with in infants a few months old, and in adults over seventy years of age.

*Sex.*—In regard to primary tuberculosis there is a great divergence of opinion as to which sex is more frequently involved, most of the English writers stating that more cases are found in men, most of the Continental writers more in women. All the more modern statistics show that the disease is unquestionably more prevalent in women, Casper stating that it is twice as frequent. Of Krönlein's 51 cases, 38 were women. In acute miliary tuberculosis Morris found, in a series of 29 cases, 18 males and 11 females. Of 46 children under fourteen years of age in Hamill's series, 32 were boys and 12 girls.

*Pathology.*—In *acute miliary tuberculosis*, both kidneys show a disseminated tuberculous infection, the tubercles appearing as minute gray nodules usually surrounded by a hyperemic zone, solitary or grouped together in cortex or medulla, the former being the favorite seat. The nodules are frequently arranged in rows following the course of the interlobular vessels, and often closely resemble small infarctions. Even in this form we may find the infection definitely limited to the areas supplied by one branch of the renal artery. It is not impossible for the bacteria to escape through the glomerular bloodvessels, especially if the walls should be injured, setting up changes in the uriniferous tubules and renal pelvis—Cohnheim's excretion tuberculosis. The changes are most likely to be noted in the interstitial connective tissue, where the characteristic cell proliferation, formation of giant cells, etc., can be seen, with associated degenerative changes in the adjoining parenchyma. Necrosis and caseation are not common because of the early death of the patient in the majority of cases.

In *primary renal tuberculosis* it is common to make a division along pathological-anatomical lines, according to which portion of the organ is most markedly affected. König describes two forms, the solitary, in which there is no connection with the renal pelvis, and the pyelitic. Israel makes three divisions: phthisis caseosa, frequently associated with perinephritis and paranephritis, and often leading to pyonephrosis; tuberculous ulceration of the points of the papillæ, much less common, but if present associated with a tendency toward severe hemorrhage; and the chronic disseminated tuberculous form, resembling the kidney of acute miliary tuberculosis, except that the disease is unilateral, the tubercles are larger, and the later processes of necrosis and caseation are more likely to be seen. Oppel differentiates cortical and medullary tuberculosis, while Tuffier divides the tuberculous infiltrations into three groups—tuberculous pyelonephritis, with or without cold abscess, massive degeneration, and tuberculous hydronephrosis.

The pathological picture depends largely upon the duration, the rapidity with which the changes take place, and the accessory factors. In most cases at a later period the process affects mostly the papillæ

and the pyramids, and the pelvis is usually involved, although in some cases the disease is confined entirely to the parenchyma, in rare instances localized in one pole, which, according to Zondek, is due to the fact that it is supplied by a single large branch of the renal artery. Animal experiments and the more recent studies seem to show that in the early stages the medullary or cortical interstitial connective tissue is most likely to be first affected, the bacilli gathering in the cortical layer, in the Malpighian bodies, or in the capillaries outside the glomeruli, and extending thence as already described. Tubercles may develop in the glomeruli themselves, in the uriniferous tubules, or the renal pelvis, as well as in the interstitial connective tissue; whatever be their situation, infection may be carried secondarily to the papillæ, the pyramids, or the renal pelvis. In the secondary focus the disease may progress more rapidly, while it is possible for the primary focus to show signs of healing; this is one of the reasons why so many renal infections were erroneously regarded as urogenous, and shows how impossible it is to determine the relative age of the process in different portions of the kidney.

The kidney may undergo complete destruction—Tuffier's massive degeneration—due to early ureteral closure by downward extension of the process, and in this form the kidney is represented by a fibrous sac filled with a cheesy, greasy, or calcified mass. When the renal pelvis is involved its mucous membrane is thickened and shows ulceration, the whole surface sometimes being involved; peripylitis is not uncommon, rarely with perforation into the adjacent tissues. In the various tuberculous foci fresh crops of tubercles may develop by direct extension or by metastasis. If the ureter is more or less impermeable, a pyonephrosis may develop, this being especially likely if there is a secondary infection. A considerable portion of the kidney substance may remain intact, or the organ may be converted into a sacculated mass, the abscesses or cavities being separated by bands or bars of renal tissue; the whole medulla and a large portion of the cortex may be converted into a large cavity, or the kidney may be changed into a shrivelled-up, putty-like mass, due to complete and permanent ureteral closure. Cheesy abscesses, whether large or small, may become inspissated, undergo calcareous change, or be discharged into the renal pelvis, causing a marked and characteristic change in the urine; as a rule, tubercle bacilli are found in these discharges, often in nests or clumps, and sometimes shreds of renal tissue. The kidney usually is enlarged to a greater or less extent, sometimes considerably so if there is marked obstruction to the flow of urine and we may have a hydronephrotic or pyonephrotic sac; a polycystic tuberculous kidney has also been described.

*Perinephric and paranephric inflammations* are quite common in renal tuberculosis, the infection being either by direct extension or by metastasis, the former being more usual.

Changes in the *ureter* are very frequent, especially in those forms in which the renal pelvis is involved, and are almost always present in the later stages. If ulceration of the mucous membrane of the renal pelvis is present it is likely to extend down the ureter, which may be dilated in its upper part, while farther down it may be more or less impermeable,

due to the inflammatory process. The mucous membrane of the ureter may show fresh tubercles, œdema, swelling, and areas of ulceration, while it is not at all uncommon for the periureteral tissues to participate in the inflammatory process. In some cases the major portion of the ureter may be unaffected and the diseased process mainly confined to the lower portion, especially the ureteral mouths, which may be of abnormal shape, the surrounding mucous membrane being either reddened or œdematous, or showing definite tuberculous changes. Hallé and Motz, from a study of the pathological preparations at the Necker Hospital in Paris, found that the disease was in some instances entirely confined to the ureteral mucous membrane; sometimes *ureteritis obliterans* was met with and frequently changes in the ureteral mouths and periureteritis. In Roberts' 32 cases of renal tuberculosis the ureters were diseased in 30.

The *bladder* is involved in a large number of cases of renal tuberculosis, although it is surprising for how long a time it may remain unaffected; in the later stages it is practically always diseased. The changes may be limited to the area surrounding the ureteral openings, or may be more extensive, in some cases the entire mucous membrane being involved. In Roberts' series the bladder was involved in 21 and the urethra in 7 of 32 cases.

The *other kidney* may remain absolutely normal or may be infected from the one primarily diseased. The infection of the second kidney may be metastatic or in rare instances, according to many observers, the infection may arise from the bladder by direct extension through the ureter or by the urogenous route, this latter mode of involvement being denied by many careful observers, and unquestionably of extreme rarity. The second kidney may show signs of compensatory hypertrophy, chronic interstitial changes, or amyloid degeneration; Albarran describes the following pathological conditions which may be referable to the other kidney: transitory albuminuria, persistent albuminuria, nephritis, hemorrhagic nephritis, and simple cylindruria.

*Unilateral or Bilateral Involvement.*—There is, as might be expected, marked discrepancy as to whether the condition is more likely to be bilateral or unilateral, according as the figures are obtained from autopsy records or from clinical observations. In a series of 12,732 autopsies, bilateral involvement was present in 62.3 per cent., unilateral in 37.6 per cent., while in some of the older series, in which obviously the disease was not studied until very late, bilateral involvement was frequent; in Roberts' series of 32 cases, 19 were bilateral, 13 unilateral.

In the more modern clinical statistics, however, there is a marked preponderance of unilateral involvement. Douglas found this to be 80 per cent.; Bevan, 90 per cent.; Albarran, 91 per cent.; Mirabeau, at least 50 per cent.; Krönlein, 92 per cent.; Israel, 92 per cent.; Kümmell, 88 per cent.; and Facklam, 91 per cent. As regards the frequency of involvement of the two sides, Küster's series of 368 cases showed the right side alone involved 189 times, the left side alone 163 times, both sides 16 times; most figures show this preponderance of the right side.



In 6000 autopsies at the Pathological Institute of Prague, 1317 were tuberculous, and of these 5.6 per cent. showed renal involvement; in 3424 autopsies at the Massachusetts General and Boston City Hospitals there were 24 cases of caseous renal tuberculosis; Rillet and Barthez found involvement of the kidneys in 49 of 315 tuberculous children; Dickinson, in 300 autopsies on subjects over twelve years of age, found renal tuberculosis 11 times; in 300 under twelve years of age, 49 times; in 2410 autopsies at the Middlesex Hospital there were 29 cases of miliary and 15 of primary renal tuberculosis. According to Wagner, surgical or primary renal tuberculosis is present in about 10 per cent. of all cases of tuberculosis. The proportion of cases which show renal involvement should in all probability be larger than those given in the figures above, in which the main dependence was upon the macroscopic appearance.

**Symptoms.**—*In acute miliary renal tuberculosis* characteristic symptoms referable to the kidney are rarely present; oliguria and albuminuria may be due to renal involvement or be but a sign of general infection; hematuria is frequently met with; tubercle bacilli, although usually found if carefully looked for, may not be indicative of any marked involvement of the kidneys, as they are found in the urine in most cases of general miliary tuberculosis and advanced phthisis; lumbar pain may be complained of, but is not uncommon in general infections. As, however, the renal disease is but a part of a general miliary infection, or appears as a terminal infection in severe lesions elsewhere, our inability to determine whether the kidney is involved is of little moment.

*In chronic or primary renal tuberculosis* the conditions are very different, the whole future of the case depending upon a prompt and clear recognition of the symptoms. Unfortunately symptoms referable to the kidney may be absolutely wanting at first, the patient only making complaint when the bladder becomes involved or the constitutional disturbances are very evident. The clinical course may be divided into four stages: (1) The latent stage; (2) from the involvement of the pyramids to the infection of the bladder; (3) the stage of bladder involvement; and (4) that of the infection of the other kidney. In the later stages diagnosis, as a rule, should not be difficult, but a successful issue depends on our being able to make an early diagnosis, and it is, therefore, the early symptoms that are especially important. In the majority of cases careful questioning and a thorough investigation will reveal some symptoms suggestive of renal disease. It is possible, however, for the disease to run an absolutely silent course, even until the kidney is completely destroyed, while the length of the latent period depends upon whether the involvement of the renal pelvis is early or late. Even in marked disease of the cortex there may be no symptoms whatsoever. As seen clinically the first symptoms, both objective and subjective, are usually referable to the bladder, and many cases for a long time have been regarded as simple cystitis or irritable bladder.

The most important symptoms are: (1) Changes in the urine, both as regards its flow and its physical, chemical, and microscopic constitution; (2) local swelling and pain; (3) constitutional disturbances. The first of these in the majority of cases is by far the most important.

1. **Urine.**—The first symptoms are usually disturbances of urination. There is an increased frequency, with burning, sometimes cramp-like pains, usually beginning about the middle of the flow, increasing to the end, and ceasing with the complete emptying of the bladder. This increased frequency is especially likely to be present at night, and may be due to a reflex stimulation of the bladder, an associated cystitis, or perhaps excessive acidity of the urine. As a rule, although not always, these disturbances are not severe except when the bladder is involved, when they may assume the most painful proportions, strangury, dysuria, and frequency of urination sometimes reaching an almost incredible degree. Incontinence is seen in a few cases, and Bazy regards this if present as a very important early symptom. The increased frequency may be constant or intermittent, and with the pain may unquestionably precede the involvement of the bladder for a considerable time. For this reason it is probably the most important symptom, as it calls attention to the urine and suggests the advisability of making a careful examination. Roberts reports a patient voiding on an average 160 times daily, in whom the bladder, however, was but slightly diseased; in another micturition was incessant until nephrotomy with drainage was performed. In some cases, even before the increased frequency and pain, the patient notices cloudiness of the urine.

The *amount* of urine varies markedly; according to some it may be diminished at first, while according to Guyon, Tilden Brown, and others, polyuria is a cardinal early symptom, especially nocturnal polyuria; in many cases the amount is practically normal. In the later stages the amount may be normal, diminished, or even increased according to the extent of destruction of the kidney tissue and the degree of hypertrophy of the sound kidney. When both sides are extensively involved, or when the flow from the diseased side ceases, due to stoppage in the ureter, we may have oliguria or even anuria. If both kidneys are catheterized, it is interesting to note the larger amount from the normal kidney, and its much quicker and more marked response to the taking of fluids by mouth. The various functional tests furnish information of great value.

The *reaction* is always acid unless the disease is complicated by an alkaline cystitis or pyelitis, or unless the patient is taking large quantities of alkalis. In some cases the acidity is increased. If there is an associated infection with one of the urea-decomposing bacteria the odor may be very foul, this being more likely to occur in the later stages.

The *albumin* present varies considerably in amount. It is usually small in the early stages, corresponding to the amount of blood and pus present, while later it is likely to be increased because of the frequent presence of an associated interstitial or parenchymatous nephritis in other portions of the diseased kidney. If the specimen is obtained directly from the diseased kidney, even in fairly early cases, a moderate or considerable amount of albumin is the rule.

The urine may be absolutely clear, as, for example, when the ureter is temporarily blocked or permanently closed, or when the disease is entirely confined to the cortex; the examination of the sediment, however,

is of the utmost importance, and, as a rule, it is the finding of pus cells, often red-blood cells, and tubercle bacilli that gives the diagnosis.

*Pus cells* are almost always present, although in varying amount; it is sometimes the cloudiness of the urine which first calls the patient's attention to his trouble. Pyuria is usually more marked if the renal pelvis is involved, and especially if there is an associated tuberculous cystitis, or a mixed infection, while it is not at all uncommon for the urine to become suddenly thick with pus after the rupture of an abscess into the renal pelvis.

The presence of *tubercle bacilli* is of the utmost importance, and, excepting in cases of general miliary tuberculosis or an active tuberculous process elsewhere, it is the most important diagnostic sign of primary renal tuberculosis. They may be found in the great majority of cases if the sediment obtained from a considerable amount of urine is centrifugalized and repeated examinations are made, preferably at intervals of several days. They are rarely present in large numbers, and often require very careful searching of many specimens; if the bladder is involved they are usually found with greater ease, although even here time and patience are required. Nests or clumps of the bacilli are often found embedded in the masses of pus, crumbling caseous material, necrotic tissue, and detritus which are present in the urine when an abscess ruptures into the renal pelvis. In 195 cases collected by Küster in which tubercle bacilli were searched for, they were found in 94, not found in 101, although unquestionably with greater care and persistence they could be found in a far larger proportion.

*Blood* in the urine is a very important symptom, microscopic blood being found in the great majority of cases and macroscopic blood not uncommonly. Red-blood cells are peculiarly likely to be present in the early stages, and a macroscopic hematuria may be the first sign noted. Macroscopic hematuria is usually intermittent, rarely profuse, as a rule not affected by rest or exercise, and associated with pyuria usually of moderate grade. According to Casper, hemorrhage is more likely to occur in the early stage, as the progression of the disease is associated with increasing obliteration of the bloodvessels. Tuffier, Albarran, Pousson, and others have reported cases of severe bleeding, requiring immediate operation, in renal tuberculosis, while Askanazy has reported five cases of his own and a number from the literature in which more or less marked macroscopic hematuria recurring at intervals was the earliest symptom, usually coming on suddenly and in some cases being the only sign of disease for many years; in one case sixteen, in another thirteen years elapsed before other symptoms appeared. The blood may sometimes entirely stop up the ureter, producing colicky pains, which often disappear with the appearance of worm-like blood-clots in the urine—blood-casts of the ureter. Klebs believes that these early hemorrhages may be due to an angiotoxin produced in the growth of the bacteria in the body.

*Epithelial cells* from the renal pelvis, ureter, or bladder are usually present and may show signs of fatty degeneration. *Casts* were found by Hunner in 10 per cent. of his cases, although, according to others,



both hyaline and granular casts are found much more frequently than this; they may come exceptionally from the other kidney, which may be affected by the circulating toxins. Granular amorphous masses, crumbling cheesy material, bits of kidney tissue, masses of friable detritus, often with tubercle bacilli embedded therein, fibrous tissue, and elastic fibres are occasionally found, and are of great diagnostic value.

2. **Local Swelling and Pain.**—Local swelling is an important but inconstant symptom, although in the later stages it may often be made out, or at least a feeling of increased resistance or of distension to the palpating hand, the organ frequently being less movable than in health. The presence of perinephritis or paranephritis increases the chance of finding a palpable tumor. The local swelling is usually not very marked except with pyonephrosis, hydronephrosis, or paranephric abscess.

*Local pain*, frequently absent or slight in the early stages of the disease, may occur spontaneously, may be constant or paroxysmal, sometimes a true renal colic, or may only be elicited by pressure, the former being, as a rule, more a dull ache, a sensation of fulness, dragging or pressure, or a sense of soreness than a severe pain. This is usually due to stretching of the capsule, and may radiate to the bladder or thigh. Tuffier's *forme douloureuse* with neuralgic pains in the renal region is extremely rare. Bazy finds three points where pain may be produced by pressure, para-umbilical, subcostal, and lumbar, while pain and tenderness in the costovertebral triangle is common if there is much perinephric or paranephric involvement. In some cases the pain, as well as the swelling, is referred to the healthy kidney which has undergone compensatory hypertrophy.

3. **Constitutional Disturbances.**—These are usually present, although, as a rule, not marked until fairly late. It is not uncommon to find a gradual impairment of the general health, diminishing strength, fatigue on slight exertion, and unaccountable dyspnoea. In other cases, but these are rare, the constitutional symptoms may develop rapidly and the picture resemble typhoid fever; such a resemblance is not uncommon in the later stages. As a rule, the constitutional disturbances develop gradually, while in some cases the condition may persist for a long time, with no apparent impairment of the general health. In the later stages the constitutional symptoms are marked—emaciation, anemia, cachexia, anorexia, and other digestive disturbances, fever, chills, and profuse sweats. These symptoms are usually more severe and develop more rapidly if the bladder becomes involved, or if there are signs of active tuberculosis elsewhere, and it is always important to determine whether some of the symptoms at least are not referable to an active lesion outside the urinary tract. In rare instances primary renal tuberculosis may develop with the typical symptoms of acute nephritis, œdema, nausea, vomiting, oliguria, etc.; œdema may also be present in the later stages, especially if both kidneys are involved.

*Fever* is present in a fair proportion of the cases, although often absent during the latent stage. According to Israel, fever is present in only 22 per cent. of the cases of uncomplicated renal tuberculosis, and in 80 per cent. if the bladder is also involved; but these figures, especially

the former, are too low. In the early stages fever, if present, is likely to consist simply of a regular or intermittent evening rise of one or several degrees, generally after exercise, while in the late stages, especially if associated with marked bladder involvement, it is usually irregularly intermittent, remittent, constant, or of the hectic type, in this latter instance profuse sweats being a common accompaniment, especially night sweats, while in some cases frequent chills occur.

*Digestive disturbances* are frequent in the later stages, while diminution of appetite is a not uncommon early symptom. In advanced cases marked gastro-intestinal disturbances are common.

*The pulse* is rapid if nephritis is present or in advanced cases, its rate otherwise being dependent upon the degree of fever. Reitter believes that hypotension of the pulse is of importance, as he found it in 6 of 10 cases of renal tuberculosis even with marked evidences of nephritis. *Anemia*, oligemia, oligochromemia, or oligocythemia is present in all advanced cases, and may appear rather early; in uncomplicated cases the leukocytes, as a rule, are either normal or diminished, the neutrophiles being especially reduced, while if there is a secondary infection, leukocytosis is the rule. If both kidneys are markedly diseased, the freezing-point of the blood may be less than  $-0.6^{\circ}\text{C}$ .

**Course.**—The course of primary renal tuberculosis is chronic and may last months and even years; the disease, while progressive, often develops so slowly that no changes may be noted in long periods of time. The difficulty or inability of determining the exact beginning makes it impossible to tell the exact duration, but from the first appearance of symptoms to the end, five or more years may elapse, and in some cases symptoms have been present for more than ten years. In half of Krönlein's cases the symptoms had been present one year, in the other half two to four years or longer, while in Kelly's group of 62 cases the average duration was three and a half years, one patient having had definite symptoms for thirteen years, yet showing on operation some secreting tissue in the diseased kidney, and the other kidney normal. A number of complications may occur; the perinephric and paranephric tissues frequently show involvement, often associated with increased pain, swelling, and severe constitutional disturbances, while disease of the ureter and bladder is extremely common. The other kidney may show toxic changes, a simple pyelitis, or typical tuberculosis. The picture may be confused by the development of a ureterovaginal or vesicovaginal fistula, while by metastasis or direct extension other organs may be involved in the tuberculous process, or the cheesy abscesses may rupture externally or into the neighboring organs.

The *cause of death* may be exhaustion or septicemia, the latter being especially likely to occur if the paranephric tissues are extensively diseased, or if there is a severe mixed infection; metastatic tuberculosis of other organs, as most commonly the lungs, the intestines, the peritoneum etc.; amyloid disease; extension of the disease to the tissues surrounding the kidney, with abscess formation and subsequent rupture, and in very rare instances uremia, the latter occurring when both kidneys are diseased,

or in some cases when one is removed and the other is tuberculous, shows signs of nephritis, or is absent altogether.

**Diagnosis.**—The realization that renal tuberculosis is usually unilateral, that its origin is almost exclusively hematogenous, and that it is a disease very susceptible to treatment if recognized early, makes the necessity of a prompt diagnosis of the utmost importance; in fact, if a cure is to be hoped for, early diagnosis is essential. It is important that we should make the diagnosis, if possible, before the appearance of marked constitutional symptoms and involvement of the bladder. This may be extremely difficult from the quiet afebrile course of the latent stage and its marked freedom from striking symptoms. It is necessary to consider carefully the family history, the past history, the general appearance of the patient, the presence of pain, dysuria, polyuria, hematuria, increased frequency of micturition, etc., to examine the urine thoroughly, to use the cystoscope and ureteral catheter, to make careful bacteriological studies, and in some cases to give tuberculin.

It is a good practice to look for tubercle bacilli in every acid, sterile, purulent urine, and to suspect renal tuberculosis in cases of slight urinary disturbances or constitutional disturbances with no apparent cause. Physicians should pay more attention to complaints of lumbar pain localized in one side and persisting for some time. The possibility of a tuberculous origin should be remembered in every case of renal hematuria without definite cause. It must not be forgotten that chronic gonorrhœa, renal calculus, or neoplasm may be associated with tuberculosis, and the discovery of the former does not necessarily exclude the latter. To make a positive diagnosis tubercle bacilli must be found in the urine, and proved to come from the kidney, while if this is not possible a presumptive diagnosis may be often made from the local pain and swelling, sterile renal pyuria, renal hematuria, and tuberculous lesions elsewhere.

*The study of the urine* gives, as a rule, the most important signs, pyuria, hematuria, and the finding of tubercle bacilli giving the diagnosis in the majority of cases. The urine should be obtained by catheter to avoid contamination with the smegma bacillus, while, whenever possible, separate specimens should be obtained by the ureteral catheter. The urine should be studied with special care when increased frequency, especially nocturnal, and pain on urination has been noted, and also, according to many clinicians, in cases of polyuria with no apparent cause. Red-blood cells are usually present, although often only demonstrable microscopically, while macroscopic hematuria is often very abrupt both in its onset and its disappearance, and may occur intermittently. *Pyuria* is usually present and of great importance.

The finding of *tubercle bacilli* in the urine gives the diagnosis if proved to be derived from the kidney, which is easy when ureteral catheterization is possible. We must not forget that they may be met with in the urine, however, in the case of active tuberculosis elsewhere. If the urine is obtained by ureteral or urethral catheterization the ordinary means of staining and studying the bacteria are all that is necessary, but if voided specimens are examined the tubercle bacillus must be differentiated from the smegma bacillus. This may be done either by animal inoculation



or by certain staining methods. Ekehorn found tubercle bacilli in every one of his 55 cases by careful search, although according to Casper they can be found in but 70 to 80 per cent. of all cases. Personal experience agrees with that of Ekehorn, although it is often necessary to make frequent examinations of the centrifugalized sediment. In suspicious cases where they are not found, guinea-pigs should be inoculated with the sediment, and, if it contains tubercle bacilli, in from four to six weeks definite tuberculous lesions will develop.

*Functional tests of the urine* from the separate kidneys should always be made when possible, although it is well to remember that a tuberculous kidney may give almost normal readings; however, the figures from a kidney with advanced disease in the majority of cases are low.

By *cystoscopy* we can determine whether the bladder is involved, and the character and extent of the disease, while by studying the condition of the ureteral openings and the contiguous mucous membrane the unilateral or bilateral character may be determined with a fair degree of accuracy, this being greatly helped by watching the urine flowing from each ureteral orifice; in some cases this urine may be studied. A dislocated, retracted ureteral mouth surrounded by reddened or swollen mucous membrane or by distinct ulcerations is very suggestive of tuberculous disease of the corresponding kidney, especially if the bladder shows slight involvement elsewhere. A cloudy or bloody urine from one ureteral orifice will often give the diagnosis, while the functional ability of the two sides may be gauged to a certain extent by the relative amounts flowing from each; if the bladder is much diseased, chromocystoscopy is of great value in helping us to find the ureteral orifices.

*The ureteral catheter* should be used if possible in every doubtful case. Albarran and Nitze shut off the diseased side with a large catheter, and thus obtain urine from the other side without catheterizing its ureter, but this is only of value when the bladder is not involved. There is frequently considerable difficulty in introducing the catheter into the diseased side, while if definite ureteral stricture is present considerable force may be necessary, the finding of such a stricture being a very important sign of renal disease. By the ureteral catheter the presence of the two kidneys can be verified, and the urine from the two sides studied separately.

*An exploratory nephrotomy* may be necessary if the cystoscope and ureteral catheter cannot be used.

The *x-rays* are sometimes helpful in showing that the kidney is enlarged or thickened although of more value in the differentiation of renal tuberculosis from calculus. *x-ray* pictures of the kidney after collargol injections through the ureter should also be employed.

The finding of a *thickened ureter* by vaginal examination is much more frequently met with in tuberculosis than in any other renal lesion.

*Tuberculin* may often be employed in doubtful cases, the subcutaneous method being more satisfactory than the ophthalmic or skin reaction or the methods by suppository or inunction. Froment has recently reported 100 cases in which the agglutination test of Arloing and Courmont was used successfully. As in all cases of renal tuberculosis there

is some focus, albeit a small one, of the disease elsewhere; it is necessary to obtain a local as well as a febrile reaction to confirm the diagnosis.

**Differential Diagnosis.**—The conditions for which renal tuberculosis may be mistaken are pyelitis, pyelonephritis, empyema of the renal pelvis, calculus, renal cancer, hypernephroma, cystic kidney, and essential hematuria. Renal cancer and calculus are most likely to cause confusion, while it must not be forgotten that in some cases these diseases and tuberculosis may coexist. In *calculus*, pyuria, as a rule, develops slowly, colic is frequent and usually severe, the pain extending down the ureter and being associated with profuse sweats. A frequent, scanty, high-colored, scalding urine, with gritty particles, is passed sometimes after the attack. Usually there is no evening rise of temperature, and the general nutrition is well preserved, while the hematuria and pain are lessened by the recumbent position and are usually intermittent. The *x*-rays and the wax-tipped catheter may definitely decide the diagnosis. In *malignant tumors* of the kidney or its pelvis the bleeding is often profuse, with no apparent cause, and with a marked tendency to intermit; the urine is often normal, pyuria being far less common than in tuberculosis; pain is unusual, swelling is common, while in the later stages cachexia is present. *Pyelitis* or *pyelonephritis* due to the pyogenic bacteria may occasionally simulate renal tuberculosis, but the presence of the bacteria and, in the cases with marked suppuration, the higher fever and more severe constitutional symptoms should make the diagnosis easy in most cases. The possibility of *hypernephroma* must not be forgotten if the *x*-ray and bacteriological examination are negative and tumor is present.

*Hematuria* without pain may also be met with in *chronic interstitial nephritis*, renal angioma, floating kidney, hydronephrosis, certain tropical diseases, and, from no apparent cause, the so-called idiopathic or essential hematuria. In urethral hematuria the urine is usually bloody at first and later clear, in vesical hematuria clear or lightly tinged, and then progressively darker, while in renal hematuria the urine, as a rule, is uniformly colored; the source of the blood cannot be determined definitely by these means, however, but only by the use of the cystoscope and the ureteral catheter. Great vesical tenesmus with increase in the frequency of urination points to cystitis, but does not exclude renal disease.

In uncomplicated tuberculosis *leukopenia* is the rule, while in all septic processes due to mixed infection leukocytosis is usually met with. Anemia is more common in renal cancer and tuberculosis than in calculus. The low blood-pressure described in renal tuberculosis may help in making a diagnosis. Secondary involvement of the adrenals may play some part in the production of leukopenia and low blood-pressure.

**Prognosis.**—This depends on a large number of factors—upon whether operation is or is not performed; upon the stage of the disease, whether it is unilateral or bilateral, whether the ureter and bladder are involved, and whether there is any active tuberculosis elsewhere; the prime requisite for a favorable prognosis is an early diagnosis. The prognosis is unfavorable if the disease is let alone, although there is some discussion regarding the advisability of immediate operation at an early stage. Pathological

anatomy shows that healing may occur spontaneously, although Küster has been able to find but one case where a spontaneous cure could be proved clinically. In rare instances the kidney may be completely destroyed and remain encapsulated. Several writers have reported spontaneous recoveries, and Godlee and others insist that if climatic and hygienic treatment were tried in the early cases a number would be definitely cured. Albarran, however, denies that a spontaneous cure has ever taken place, and Kelly has never seen a medical cure, although in a number of early cases he tried rest, forced feeding, fresh air, etc., for a number of months.

The exact status of tuberculin therapy or treatment with attenuated living bacteria has not been determined, but if it should prove successful, early renal tuberculosis should prove a useful field for this mode of treatment. At the present writing, however, it seems that as the prognosis is unfavorable if let alone, as cure is improbable under general hygienic treatment, and as the chances of recovery are so much lessened by delay, early operation is *the treatment* for primary renal tuberculosis, if we can determine definitely the presence, the functional ability, and the freedom from disease of the other kidney and the absence of extensive tuberculosis elsewhere. However, we must not forget that this form of renal disease is always secondary, and that even after its removal the patient for a considerable period of time should be carefully treated in the hope that the primary focus may become entirely healed. It is surprising in how many cases bladder tuberculosis is susceptible of successful treatment after the removal of the diseased kidney.

**Treatment.**—The general *prophylaxis* is the same as in tuberculosis elsewhere—fresh air, sunshine, good food, keeping the nutrition of the body at its highest point, and lessening as far as may be the chance of exposure to the germs of tuberculosis. If tuberculosis should be present in the body it should be treated as early as possible along the approved lines. The special prophylaxis consists in removing at once any focus of tuberculosis that may be present in the body, in the epididymis, glands, joints, bones, etc., and to obviate all existing conditions which tend to lower the resistance of the kidney, especially diseases of the urethra, prostate, and bladder, gonorrhœa, etc.

The present attitude is that in the vast majority of cases surgical treatment offers the only hope of real cure, and that the earlier this treatment is inaugurated the better the chance of recovery. It is beyond question that at the stage in which the disease is usually recognized the condition will advance under any other form of treatment, and it is only those cases in which an extremely early diagnosis is made in which general treatment would be at all justifiable. We realize that amyloid disease or toxic nephritis of the other kidney will render the prognosis much less favorable, and will usually preclude operative treatment. It is therefore important to remove the source of the toxins before such changes occur, while the longer the operation is postponed the greater the chance of a more general tuberculosis and the less the chance of recovery when operation is performed. The older view was that active tuberculosis elsewhere, especially in the lungs and the bladder,



was a distinct contra-indication to operation, but more recent work has shown that in the case of the latter even extensive disease is no bar to nephrectomy, while in the case of the former, although in general an advanced active lesion would preclude operation, yet in a number of less active and not so advanced cases distinct improvement may follow the removal of the kidney. If the symptoms referable to the kidney and bladder are very marked, and the pain, tenesmus, increased frequency of urination and constitutional disturbances are making life a burden to the patient, it is justifiable even in advanced cases to take some risk in the hope of ameliorating the condition.

**Surgical Treatment.**—The operations which may be considered are nephrectomy, nephrotomy, nephrostomy, and partial resection of the kidney, although the first of these is always the operation of choice if the circumstances warrant it—that is, if the other kidney is healthy and the general condition of the patient is such as to warrant the operation.

In *nephrectomy* it is of paramount importance that the presence and healthy condition of the other kidney be determined. According to Rovsing, the absence of albumin, pus, or bacteria from the second kidney may often be relied upon; if pus and bacteria are present, removal of the first kidney is usually contra-indicated, while if albumin but no pus or bacteria is found, it is not a contra-indication, the albuminuria being due to toxic changes and usually disappearing rapidly after the removal of the diseased organ.

Kümmel divides renal tuberculosis into three groups, surgically speaking: (1) The early stage, when operation can be done; (2) when one kidney is severely and the other slightly diseased, and here, according to Kümmel, if the freezing-point of the blood is  $-0.56^{\circ}$  to  $-0.57^{\circ}$  C., the more seriously diseased organ may be removed, while if  $-0.6^{\circ}$  C., nephrotomy must be done; (3) where the ureteral catheter cannot be used, and here an exploratory nephrotomy should be done, and from the findings and the cryoscopic index of the blood the proper treatment can be decided upon, but most surgeons do not rely on blood cryoscopy as Kümmel does.

The extraperitoneal operation should always be done, while if the perinephric and paranephric tissues are markedly involved some surgeons do an extracapsular rather than the more common intracapsular extirpation. There is always some danger of the shock, depletion, and other constitutional disturbances incident to a severe operation, lighting up a tuberculous focus elsewhere, but experience shows that this is unusual. Pregnancy is not a contra-indication. If there are other secondary tuberculous lesions, such as in the epididymis, glands, etc., or if the primary foci can be determined they should be removed at the same time if possible. If tuberculosis is advanced elsewhere, nephrotomy or nephrostomy is often a preferable operation, while if after this operation the fever, constitutional symptoms, etc., disappear or markedly abate, a secondary nephrectomy may be done if the ureteral catheter and the functional tests show the other kidney to be healthy.

According to Kelly the ureter, if diseased, and the portion of bladder about the ureteral opening, if involved in the tuberculous

process, should be removed at the same time as the kidney, or at a later operation if the patient's condition does not warrant it being done primarily. Kümmel inserts a platinum needle into the lumen of the ureter from above and heats it to a white heat, and Bevan cauterizes the ureteral mucous membrane with pure carbolio acid, although some surgeons believe that the ureter had best be let alone, as it usually heals after removal of the kidney. In some cases, however, a persistent sinus is left, while in other cases it is impossible to cure the bladder until a secondary ureterectomy is done.

Involvement of the bladder, even if advanced, is no contra-indication to nephrectomy. Sometimes after nephrectomy the bladder heals spontaneously, while if tuberculous cystitis persists, besides the usual constitutional measures local treatment may be employed, Rovsing finding that instillation of solutions of carbolio acid, 5 to 6 per cent., is the most effective local treatment. In very severe cases draining the bladder and the use of the constant bath may be necessary.

*Nephrotomy* or *nephrostomy* is only justified when the patient's condition is such that a nephrectomy is impossible, when both kidneys are involved, or when ureteral catheterization cannot be performed. After the nephrotomy, if the condition of the patient markedly improves, as is often the case, and if we have been able to determine the functional ability of the other kidney, a secondary nephrectomy is advisable in many cases.

There is a great temptation to do a *partial resection* or *partial nephrectomy* if the tuberculous focus seems definitely localized, and this has been done with success; but in the great majority of cases some tuberculous foci are left behind in the parenchyma, and for that reason the weight of evidence is in favor of absolutely abandoning this operation in favor of total nephrectomy except in rare cases of bilateral disease where it seems to be more indicated than nephrotomy.

In the case of perinephric abscess secondary to renal tuberculosis, opening and draining the abscess is all that is done at first, while later secondary nephrectomy may be necessary. After the former operation, as well as after nephrotomy, persistent fistula is not uncommon.

*The results of operative treatment* both as regards immediate and ultimate result have been in the main favorable, although figures in the latter connection are more difficult to obtain and are often less definite. The operative mortality, which formerly was from 20 to 25 per cent., is now from 3 to 10 per cent. Casper found that in the practice of five surgeons before the use of the cystoscope, the ureteral catheter, and the functional tests, the mortality in 139 cases was 21.7 per cent., while after the use of these methods the mortality in 130 nephrectomies by the same surgeons was 10 per cent.; Rovsing, in 112 nephrectomies, has reduced his mortality from 13 to 3.3 per cent. As regards the ultimate results of nephrectomy, the figures are very encouraging. Kümmel reported that 32 of 43 patients were living and well some time after the operation; Albarran was able to follow 39 for a considerable period of time, and only 5 died of tuberculosis; Kelly got a complete cure in all of 21 patients in whom the bladder was not involved, and in 18 of 36

where it was extensively diseased, the cures being from two to twelve years; Israel in 29 cases got cures of from one to nine years in 11; Küster, 11 complete cures of from one to seven years in 17 cases; Schede, 16 cures of from one to ten years in 22 cases; and Czerny, 11 cures of from one to twenty-one years in 27 cases, in 16 of which secondary nephrectomy was done.

As regards nephrotomy, in a series of 72 cases from different surgical clinics, 7 were cured completely, 18 had a persistent fistula, 28 required a secondary nephrectomy, and 21 died. As regards kidney resection, few figures are obtainable. Morris reports 7 cases with 4 cures of from two to four years.

**Medicinal, Climatic, and Hygienic Treatment: Tuberculin.**—Some believe that it is advisable, if an early diagnosis can be made, to first try general treatment, as a cure is theoretically possible and a small number of clinical cures have been reported. It would be most interesting to treat a series of very early cases by climatic, dietetic, and hygienic measures, and this would be comparatively safe if the weight, temperature, general and local condition, and the urinary findings were watched with extreme care, so that at the first sign that the disease was progressing operation could be done at once. Recently there has been a distinct feeling that specific treatment may prove successful. Birnbaum used tuberculin in the treatment of 23 cases of renal tuberculosis, and found it most helpful, although only in the very early cases in which fever was absent.

**Symptomatic Treatment.**—When cure is impossible it is important to make the patient physically comfortable by careful attention to both the general and the local symptoms, and such care may be rewarded by considerable temporary improvement. The pain must be relieved, in some cases by simple analgesics, in others by opium or morphine; occasionally severe hemorrhage must be controlled; the fever may be reduced by sponging or by antipyretics. In all cases a generous, nutritious dietary, a proper climate and attention to the personal hygiene should always be insisted upon. When the bladder is diseased, irrigation, topical application, and hydraulic distension may be employed; while if the pain and tenesmus are intense, it may be necessary to open and drain the bladder.



## CHAPTER XIX

### TUMORS OF THE KIDNEY

By HUGH HAMPTON YOUNG, M.D.

**Hypernephroma.**—In the discussion of this subject there is much confusion, owing to the various names that have been used by different authors for the same tumor, viz., perivascular sarcoma, venous endothelioma, lymphatic endothelioma, epithelioma with clear cells, adenoma with clear walls, etc. The descriptions and illustrations which have been given all bear such a striking likeness to the tumor now called hypernephroma that these names should be discarded until a precise nomenclature can be agreed upon.

**Etiology.**—In a series of 176 cases of hypernephroma collected from the literature by Garceau, the *age* at which the disease occurred varied from eighteen months to eighty years; by far the largest number (60 per cent.) occurred between forty and sixty years of age.

**Pathology.**—The first accurate description of the pathology of the tumor was published by Grawitz in 1883, and it was he who first considered that it arose from aberrant adrenal tissue, which is so frequently found in the kidney. Previous to this the tumor was supposed to be a variety of lipoma. In 1894 the name *hypernephroma* was suggested by Lubarsch. Grawitz made no attempt to classify the growth, saying that at times it resembled adenoma, at others sarcoma, and at others carcinoma; but he gave the following reasons for his belief in its adrenal origin: (1) The position of the growth under the capsule where adrenal “rests” are generally found; (2) the resemblance of its most characteristic cell to those of the adrenal; (3) the characteristic fatty infiltration of the tumor cells of the adrenal, which is a constant feature of the cortical cells of the adrenal, but is never seen in the normal renal cortex; (4) the presence of a capsule which separates it from the adjacent kidney substance; (5) the arrangement of cells in columns, as in the fascicular portion of the adrenal cortex; (6) the amyloid degeneration in the blood-vessels, which is rarely seen in other tumors, and the fact that the metastases from these renal tumors exactly resemble those of tumors which are definitely of adrenal origin.

Since the publication of Grawitz there has been much discussion and confusion in the literature in regard to the histogenesis of these tumors which will be found in Garceau's work on *Tumors of the Kidney*.

The occurrence of adrenal rests has been the subject of considerable study. Imbert found them in different organs in 92 out of 100 autopsies, in the kidney in 8 per cent. of the cases. Wilson and Willis<sup>1</sup> consider

<sup>1</sup> *Jour. Med. Research*, vol. xxiv, p. 73.

that most if not all so-called "adrenal rests" are probably of Wolffian origin. They state that there is almost no evidence, embryological or histological, in support of Grawitz's hypothesis that the so-called "hypernephromas" have their origin in adrenal rests, but contend that these tumors arise from islands of nephrogenic tissue (primitive renal blastema). They state that such tissue is sometimes present in the adult kidney and appears capable of forming tumors of the non-infiltrating mixed tubular, papilliform and sarcoma types, so characteristic of the so-called hypernephromas.

The location of hypernephromas in the kidney is usually in the upper pole, just beneath the capsule. There may be one nodule or several, which may be small or large, the whole tumor varying in size from that of a pea to that of an adult human head. They are usually encapsulated and sharply contrasted with the surrounding or adjacent renal tissue, which often shows evidence of atrophy and interstitial nephritis. The consistence in the smaller tumors is often firm, but when the tumor is large it is usually soft, and blood-cysts are often seen. Areas of more or less extensive hemorrhage in the tumor tissue are found on section, and large areas of necrosis are common.

**Histology.**—The similarity to adrenal tissue is most marked in the small hypernephromas. The stroma is largely composed of capillaries upon which the cells lie without intervening tissue, ranged in rows, sometimes two or three deep. These cells are, as a rule, rather larger than the normal adrenal cell, polygonal in shape, and contain much fat. Giant cells and karyokinetic figures are sometimes seen. Chemical examination reveals glycogen and lecithin, which along with fat are also found in normal adrenal cells. In the large tumors there is a certain amount of fibrous tissue in the capillary stroma, and the polygonal cells are often arranged in distinct alveoli. This alveolar arrangement has given rise to the opinion that the disease is a carcinoma or an alveolar sarcoma. Papillary formations are also seen, and the arrangement in rows is composed of more cells than in the small tumors. In the larger tumors necrosis not infrequently occurs, generally in the centre of the mass and most remote from the peripheral blood-supply.

**Invasion.**—The tumor may be only a small nodule in an otherwise healthy kidney. With time, however, the tumor invades the kidney more and more, causing first a pressure atrophy, finally in some cases completely replacing the kidney and forming a large lobulated irregular mass which is usually completely encapsulated. Neighboring structures may be invaded, but this is rare, as is also invasion by the lymphatics. As a rule, the systemic invasion is through the veins. It is not uncommon to find the renal veins invaded by the tumor, which may conform to the shape of the vessels and grow intravenously to great distances. In one of the writer's cases the vena cava was filled with a non-adherent growth, which extended upward through the diaphragm and down to the brim of the pelvis. The renal vein on the opposite side was invaded almost up to the kidney. Another case is reported in which the thrombus extended into the auricle of the heart. Loosened emboli are carried through the blood-current to remote portions of the body. Metastases

have been found in the brain, bronchi, diaphragm, heart, liver, intestines, omentum, pancreas, pleura, peritoneum, skin, uterus, urethra, and in various portions of the bony skeleton. These metastases reproduce exactly the histological characteristics of the parent tumor. In rare cases the tumor mass grows out into the renal pelvis, but no case has been found in which the ureter was invaded.

**Symptoms.**—Hypernephroma is so variable in its growth that the symptomatology is by no means uniform. Many of the cases in which the tumor is small, benign in its character, and very slow of growth, may present no symptoms, and in such cases the tumor is often discovered postmortem. In others a small tumor may be accompanied by abundant symptoms, and if at the lower pole of the kidney may be detected by palpation. In those cases in which the tumor assumes a malignant character the growth may be rapid and the symptoms marked. The three cardinal symptoms are hematuria, pain, and tumor.

**Hematuria.**—This is the most frequent sign of malignant tumors of the kidney in adults. In 83 cases reported by Desnos, hematuria appeared before every other symptom in 41 cases; Israel places it at 70 per cent.; Denoclar at 65 per cent.; Albarran at 54 per cent., and Küster at 52 per cent. Garceau found hematuria a prominent symptom in 50 per cent. of 106 cases, but in 35 cases it was absent. In some it is the sole symptom, and in one of Israel's cases was present for twelve years.

Generally the bleeding comes on insidiously and continues several days, after which it may not reappear for several months. The attacks become more frequent, as a rule, with the progress of the growth, and often recur with regular periodicity. The urine is usually markedly colored with blood, and frequently large clots are passed. Rarely the advent of bleeding is presaged by a dull pain in the side, sometimes simulating renal colic. In such cases the ureter has usually become blocked by a clot, and for a time the urine voided may be free from blood. This is usually followed by cessation of the pain, accompanied by the sudden reappearance of blood and the passage of clots.

Statistics show that the hemorrhage is not influenced by position or occupation, occurring as frequently at night as during the day. In spite of their frequent repetition, the hemorrhages rarely weaken the patient so greatly that operative intervention is necessary to stop the bleeding. The sudden change from very bloody to perfectly clear urine is of considerable diagnostic importance, showing that the ureter has become blocked. Worm-like blood-casts of the ureter are not uncommon.

**Pain.**—This is often absent for a long period, and is rather variable in its character. Many hypernephromas reach considerable size without causing any pain. In some it is merely a dull ache in the lumbar region, but occasionally the pain runs downward along the sacral and pelvic nerves. It usually comes on spontaneously without relation to exercise or bodily position, and in some cases may be quite severe for a short while. Pressure on the kidney does not usually increase the pain, but the patient is sometimes unable to lie on the affected side.

**Tumor.**—When the growth is of the voluminous type a perceptible or palpable tumor of the flank is one of the most important symptoms.



According to Garceau, tumor is usually the first sign of hypernephroma, and in 143 cases it was present in all but 17 cases. In many of the cases, in which the disease begins at the upper pole of the kidney, palpation will not detect it until late, and in a few cases in which the tumor remains small it is never discovered during life. The growth generally preserves the usual shape of the kidney, and may be uniformly smooth. Very often it is irregular, lobulated, or nodular. When the tumor is large the flank is deformed and the shape of the tumor may be apparent on inspection. In cases of moderate size it may be perceptible only on bimanual examination. The usual site of the tumor is in the lumbar region, but extending forward in the abdominal cavity, and generally lying between the ribs and iliac crest, with no space between the tumor and the lumbar muscles. Small tumors are often movable, but the larger ones are generally fixed. The x-ray has not as yet proved reliable in demonstrating tumors of the kidney. In determining the character of the tumor its relation to the colon is of great help, and the following is quoted from Garceau: "The kidney is normally situated behind the colon, and when enlarged by a tumor it must develop in the layers of the descending colon; hence the colon will be found in front of the tumor or toward its inner side. Tumors of the liver crowd the colon down and may override it; tumors of the stomach also crowd the colon down, while tumors of the pancreas almost invariably appear above the transverse colon, and in a few instances behind it. A tumor growing in a movable kidney may enter the central zone, but unless fixed it can be slipped back into position. Tumors of the adrenal push the colon forward and inward. The central region, besides uterine and ovarian tumors, may contain growths of the small gut, the mesentery, omentum, and also enlarged retroperitoneal glands. The spleen must be on the outside of the descending colon, but if greatly enlarged may override it entirely; there is no line of resonance between the kidney dulness and the vertebral spines as there nearly always is in the case of splenic enlargement. Tumors ordinarily close to the abdominal wall may in consequence of adhesions be separated from it by intestines; in this case there will be tympany in front of them. Tumors of the spleen, liver, and uterus may present these characteristics, and especially tumors of the ovary."

*Changes in the Urine.*—There are no changes in the bladder urine in any way characteristic. Hematuria may be the only abnormality. In the intervals the urine may be perfectly normal.

*Other Symptoms.*—Renal neoplasm may produce symptoms due to compression of surrounding structures. One of the most common is varicocele, and it is considered quite significant when present on the right side. In 20 cases Kapsammer found marked circulatory disturbances of the inferior membranes and of the abdominal wall. In one of the writer's cases in which the vena cava was almost completely obstructed by a large intravenous growth, the peritoneal veins were greatly dilated, and with the portal veins, which were also dilated, took care of the return circulation from the inferior extremities and the abdomen. Edema and ascites are sometimes present in such cases. Jaundice may occur, due to obstruction of the common bile duct or

extension of the disease to the liver. Only rarely does the tumor growth cause painful symptoms from compression of the nerves, and marked pain in the spine often indicates metastases. Gastric symptoms, nausea, vomiting, and occasionally hematemesis have been reported, and may indicate either metastases or uremia. Dyspnoea may be present.

*Cystoscopy.*—If hematuria is present, a jet of red urine can usually be seen to escape intermittently from the affected side. If the urine is only faintly colored, it may be impossible to detect any difference between the two sides; and if the hemorrhage is very great, it may be difficult to get a field clear enough for accurate observation. For the latter cases the "evacuation" cystoscope may be very helpful. In some cases the ureteral orifice may be abnormal—it may be dilated, as a result of the pressure of clots, or it may be surrounded by hyperemic, swollen, or oedematous mucous membrane. In some cases the simple cystoscope shows nothing definite (especially between attacks of hematuria), and ureter catheterization is advisable in order to determine the functional value of the two kidneys. A small amount of blood from either ureter is of no importance, as it may be traumatic. In determining the renal function, the phthalein test furnishes the most information. The concentration of phthalein and urea is usually equal to that of the healthy kidney, but the absolute amount excreted is decreased. Radiographs taken after injection of the renal pelvis with 10 to 15 per cent. collargol may show marked and sometimes characteristic changes in the shape, size, and character of the pelvis and calices.

*Duration.*—In a list of 27 operated cases collected by Garceau the tumor had been present for fifteen years in 1 case, twelve years in 1, ten years in 2, eight years in 2, seven years in 2, six years in 5, five years in 6, four years in 2, three years in 5 cases; but in another list of 89 cases the duration of the symptoms when nephrectomy was performed was not over a few months in 53 cases. The duration of the disease is generally shortened by the early appearance of metastases, which may be of large size, very painful, and lead to exhausting symptoms which completely overshadow the renal affection. In a series of 21 cases collected by Garceau, in which metastases were present and no kidney operation performed, it is a notable fact that in only 4 cases had the duration been more than one year when death resulted. In nearly all of these cases the metastases, particularly of the bones and lungs, were of more moment than the renal tumor.

*Diagnosis.*—In most cases the patient has not suffered from pain, and the presence of hematuria has alone attracted the attention.

The diseases most commonly confounded with hypernephroma are tuberculosis, calculus, hydronephrosis, pyonephrosis, and tumors elsewhere in the abdomen.

*Tuberculosis* of the kidney is first to be considered and excluded in all cases. In tuberculosis pus is generally present in the urine between the crisis of hematuria, and by careful search tubercle bacilli can generally be discovered. Great care must be taken to exclude the smegma bacillus. The smegma bacillus may be found in the anterior urethra, but never back of the external sphincter, and if the penis is thoroughly cleansed

and the anterior urethra irrigated, none of these organisms will be found in the voided urine. As an additional precaution, it is well to have the patient void in three sterile glasses and to make the bacteriological examination from the third glass. If bacteria are found resembling the tubercle bacillus in form and not decolorizing with acid, one can be sure that it is the tubercle bacillus. When the results are negative, the tuberculin test may be advisable.

The presence of foci of tuberculosis in other organs may be of great assistance; this is particularly true of the genito-urinary tract, as nodules in the prostate and seminal vesicles or in the epididymis are not infrequently found. Non-tuberculous renal infections are, however, not infrequently associated with prostatitis characterized by more or less extensive induration, often closely resembling tuberculosis of the prostate. The cystoscopic picture of the ureteral orifice is generally of great diagnostic worth. In tuberculosis it is apt to be dilated, often gaping, sometimes ulcerated, and surrounded by an area of vesical tuberculosis; whereas in hypernephroma only a slight hyperemia or dilatation of the ureteral orifice is seen. Tuberculosis is rarely associated with the great enlargement of the kidney often seen in hypernephroma, but in early cases the diagnosis may be extremely difficult.

*Renal calculus* may also simulate hypernephroma. It is usually more painful and the kidney less enlarged, but the writer has seen a case in which the kidney was immense and contained fourteen large stones (several larger than hen's eggs), in which there had never been pain, hemorrhage, or discomfort, and the patient sought relief because of occasional febrile attacks. The radiograph is here of great diagnostic value. Pyuria is not of great value, as it may be present in renal calculus and hypernephroma, although more common in the former.

*Hydronephrosis*, *pyonephrosis*, and *perinephritis* may all be associated with an enlarged indurated mass closely simulating neoplasm, and the occasional presence of hematuria may make the resemblance close. On the other hand, intermittent distension of the renal pelvis accompanied by tumor formation and crises of pain which are so characteristic in certain forms of hydronephrosis, the writer has seen in a case of hypernephroma. In this case during the periods of bleeding the tumor mass would occasionally become greatly enlarged. This was always associated with sudden cessation of the hematuria (evidently due to blocking of the ureter with a clot) and severe pain.

*When hematuria is the only symptom* it is often very difficult to make a diagnosis, and we must consider not only tuberculosis and calculus (both of which may present this symptom alone), but also the *essential renal hematuria* of Senator and Klemperer, the hemophilic hematuria of Senator, the hematuria of pregnancy (Guyon), and the hematuria which accompanies certain cases of chronic nephritis (Pousson).

These hematurias present a most perplexing and little understood class of renal disorders and have led to much confusion. It has been definitely shown that hemorrhage may occur from a kidney in which it is impossible to discover any macroscopic or microscopic lesion, and may reappear with such frequency and abundance as to be serious.



Some have asserted that this is almost always associated with a localized nephritis which is sometimes unilateral, but that such is not generally the case has been abundantly proved. The question of such nephritis is, however, of sufficient importance to warrant the catheterization of the ureters in all such cases, both during and between the attacks of hematuria. The writer has suggested the injection of about 15 cc. of a 1 to 3000 solution of adrenalin chloride into the renal pelvis through a ureter catheter. In three cases of essential renal hematuria this treatment was followed by a disappearance of the hematuria, which at this writing seems to be permanent. While it might be possible to completely stop the hemorrhage from a hypernephroma, it seems very probable that it would soon recur and the presence of pain and tumor would of course lead to suspicion of neoplasm.

*Other tumors* of the abdomen have to be considered in making the diagnosis, but we have not the space to do more than call attention to the usual absence of urinary symptoms in such cases and to the general principles of abdominal examination and diagnosis.

The diagnosis of hypernephroma from *other forms of renal tumor, carcinoma, sarcoma, and malignant adenoma* is often impossible.

The benign tumors *fibromas, adenomas, lipomas*, etc., are rarely associated with hematuria or pain. *Polycystic disease* of the kidney is more apt to be bilateral and free from hematuria. In later stages it is accompanied by symptoms of renal insufficiency, headache, nausea, etc., and marked decrease in total renal function, which do not often occur in hypernephroma. Radiographs of the injected pelvis in polycystic disease are very characteristic.

*Teratomas and rhabdomyomas* occur so rarely as to make diagnosis almost impossible. In hydatid diseases of the kidney, hooklets may be found in the urine.

**Treatment.**—Medical treatment, except of a symptomatic or palliative character, is of little use. An early operation should be performed in all cases where the condition of the patient admits of it, and in recognition of this fact an early diagnosis should be aimed at. When the tumor is large, operation should usually be undertaken unless complications of considerable severity, sufficient to cause the patient to be denied a chance of cure or relief, are present; for it is true that in some cases the pain is so considerable that operative relief should be afforded, even though the chance of cure is remote.

**Operation.**—Before this is attempted the patient should be in the best possible condition and the functional ability of the supposed sound kidney should be determined by ureter catheterization and the phthalein test. If the hemorrhage continues and immediate operation is not to be thought of, the injection of adrenalin through a ureter catheter may be employed. Operative technique is hardly within the scope of this article, but it may be well to state that complete nephrectomy should almost always be done, and that it may be performed either intra- or extraperitoneally. Nearly all authors are agreed that the lumbar extraperitoneal route is preferable for all but the large hypernephromas. By extending the oblique lumbar incision downward and inward it is possible

to get a very large field of operation, to see the depths of the wound, and to ligate the vessels of the pedicle separately (after carefully examining them to see that no intravascular neoplastic growths are present). It is agreed that the fatty capsule, the adrenal and adjacent glands should be removed with the kidney, if possible, but that it is unnecessary in the case of hypernephromas to remove much of the ureter.

The *intraperitoneal route* is in favor with most surgeons for large tumors, especially those in children, and with some for the smaller tumors. The advantages claimed for it are the large field obtained, the ability to palpate the other kidney, to ligate the bloodvessels of the pedicle before attempting to free the kidney from the surrounding adhesions which are apt to bleed profusely, to remove the fatty capsule, glands, and adrenal more thoroughly, and to detect thrombotic growths in the renal vein or vena cava before attempting fruitless procedures on the kidney.

*Operative Results.*—The statistics are unfortunately meagre. Garceau states that in 176 cases of hypernephroma collected by him there were 143 nephrectomies, with 33 operative deaths (occurring within two months after the operation), a mortality of 23 per cent. These statistics cover a period of fifteen years, and the mortality is probably much less now. Isreal has published 17 cases of nephrectomy for hypernephroma. Of these, 16 were operated upon by the lumbo-abdominal extraperitoneal route, with 3 immediate operative deaths from heart failure or shock. In 4 cases death from recurrence or metastases resulted in five months, eighteen months, and two years (2 cases) respectively. In all of these cases the patient was greatly benefited, although all were extensive. Eight patients were still alive and well when the publication was made. In 2 cases two years, in 2 cases six years, and in 1 case nine years had elapsed since the operation. When it is considered how long the tumor had generally been present, its size and the weakened condition of many of these patients, the results are very encouraging. With early diagnosis and prompt operation the mortality should be reduced greatly.

**Carcinoma of the Kidney.**—As a result of a more careful pathological study of kidney tumors, carcinoma has become in recent years exceedingly rare. The great histological variations in hypernephroma, the transition in various parts of the tumor to the adenomatous, carcinomatous, or sarcomatous type, often render the true nature of the tumor extremely difficult to determine. Undoubted carcinoma of the kidney is exceptionally rare, and its existence is doubted by some authors. Neuhauser<sup>1</sup> in a study of 69 tumors from Israel's clinic found that 65 were apparently typical hypernephroma; 2 of the tumors he classed as hypernephroid carcinoma and 2 as hypernephroid sarcoma. In the 2 cases designated as hypernephroid carcinoma portions of the tumors were typically cancerous and formed cell nests not unlike those seen in mammary cancer. Other portions had the typical appearance of true hypernephroma. He is very positive in his statement that all carcinomas of the kidney arise from hypernephroma. On the other hand, Garceau

<sup>1</sup> *Arch. f. klin. Chir.*, 1906, vol. lxxix.

has reported three carcinomas, about the nature of which there is apparently no doubt, while we have been able to find one true adenocarcinoma at the Johns Hopkins Hospital. This has been reported by Cullen.<sup>1</sup> Of the 4 cases which we have been able to verify, 2 were in women and 2 in men, and the ages ranged from twenty-six to forty years.

**Pathology.**—According to Waldeyer,<sup>2</sup> carcinoma of the kidney arises from a proliferation of the renal tubules. The infiltrating form is agreed, almost by common consent, to be the most frequent form of carcinoma, and of the 4 cases referred to above, 3 were of the infiltrating type, 1 only being a definite adenocarcinoma. In none of the infiltrating forms was the kidney markedly increased in size. The shape of the kidney is usually well preserved and the cancerous growth invades it quite regularly, producing a uniform enlargement. In the case of adenocarcinoma the tumor mass was somewhat kidney-shaped, irregular in outline, and about five times the size of the normal kidney. On palpation the tumor seemed to be cystic. On section no renal tissue was demonstrable, the greater part of the tumor being soft and consisting of a spongy homogeneous tissue resembling carcinoma. On microscopic section the tumor was seen to be a glandular growth; the gland type was particularly well marked and the acini were very regular in size.

**Symptoms.**—The first symptom noted in the infiltrating forms was acute agonizing pain in the region of the affected kidney, of a radiating character in one case. In the case of adenocarcinoma, a tumor mass was the first symptom. Hematuria was persistent and abundant in one case, slight and recurrent in two, and absent in one. A tumor mass was noted in three cases; in one case no enlargement of the kidney was demonstrable. The duration of symptoms varied from one to four months, and death occurred in the three infiltrating forms in from seven weeks to seven months after the onset of the first symptoms. In the case of adenocarcinoma the patient died six years after operation with extensive general metastases.

**Diagnosis.**—It is impossible to clinically differentiate carcinoma from malignant hypernephroma or other malignant forms of kidney tumor. With the exception of the early, severe, radiating pain, there is no differential point which would make one suspect the possible cancerous character of the disease.

**Treatment.**—(See section on Hypernephroma.)

**Malignant Papillary Cyst Adenoma.**—A separate classification is usually reserved for this rather uncommon tumor. It bears a close resemblance, histologically, to benign adenoma, and most frequently a papillary type of tumor prevails. While, histologically, the picture resembles closely benign adenoma, at times a distinctly malignant picture is seen. These tumors are almost always malignant and should be treated as such. The kidney is seldom much enlarged, is nodular and hard, and, on section, shows numerous small cystic areas full of a gray or deep red material. At times the growth becomes infiltrating, and in such cases gives the histological appearance of the infiltrating type

<sup>1</sup> *Jour. Amer. Med. Assoc.*, 1905.

<sup>2</sup> *Virchows Archiv*, 1867, vol. xli, p. 493.



of carcinoma. The *symptoms* and *treatment* are identical with those described under Hypernephroma.

**Adenomas.**—These may be either benign or malignant, isolated or multiple. The small multiple adenomas of the kidney are not infrequently found at autopsy, and vary in size from a millet-seed to that of a pea. They are usually found beneath the capsule, but occasionally are seen within the parenchyma of the kidney. The large variety is much more rare. On section, these tumors are grayish white in color, friable, frequently infiltrated with blood, and sometimes studded with cysts. Benign adenomas usually present no symptoms, even the large forms rarely producing any discomfort, hematuria or palpable tumor. The so-called malignant form of adenoma resembles carcinoma of the kidney so closely that it seems unwise here to attempt to differentiate them.

**Sarcoma of the Kidney.**—Many cases of sarcoma of the kidney have been described in children, but careful microscopic examinations have shown that they were almost always mixed tumors. Sarcoma is much rarer than hypernephroma in the adult. In Rosenstein's 30 cases there were only 8 in which the patient was over twenty years of age, 6 being in the period from forty to sixty years of age. In the adult these tumors do not reach the enormous size seen in children, and Albarran says that they seldom are larger than two fists in size. He recognizes three forms: (1) Those which start in the capsule and which may for a time be encapsulated and more or less separated from the kidney; (2) those in which the tumor has its origin in the region of the hilus; and (3) those beginning in the parenchyma, which are the most frequent, and are present either in an infiltrating or a nodular form.

We have had the opportunity of studying two cases of pure sarcoma of the kidney occurring in children: one was a small, round-cell sarcoma occurring in a girl eighteen months of age, and noticed eight weeks before death occurred; the other in a boy, four years of age, of a pure, spindle-cell variety, had been noticed three months before death occurred. In the case of the round-cell sarcoma, metastases were found in the lungs and in the spindle-cell sarcoma in the retroperitoneal lymph glands.

According to Garceau, the capsule is most frequently the origin of the growth from which place the soft tissues are invaded. Sarcoma of the kidney is very similar to that of malignant hypernephroma of the kidney in its progress, symptomatology, and prognosis. The tumor, as a rule, remains encapsulated and metastasis occurs through the veins. In some cases the duration of the disease is only a few months, but in other cases (particularly the spindle-cell variety) it may be several years.

**Symptoms.**—The three cardinal symptoms of renal tumors, hematuria, pain, and tumor, are found in cases of sarcoma, and it is almost impossible to make a differential diagnosis between hypernephroma and sarcoma. The treatment should consist in early nephrectomy in all cases; the prognosis even then is not good, owing to the frequency of metastases.

**Embryonic Tumors of the Kidney.**—As in the case of other organs, the kidney is subject to tumors arising from inclusions or occlusions of apparently embryonic tissue; these, however, differ somewhat from the

fetal tumors of other organs. The typical dermoid cyst of the kidney is very rare indeed, only two cases having been reported: one by Haeckel<sup>1</sup> and one by Paget.<sup>2</sup> Pure rhabdomyoma of the kidney is also extremely rare. The typical *mixed* tumor of the kidney is, however, not a very rare occurrence in children. The histogenesis of the tumor is rather indefinite, Weigert claiming that they arise from the Wolffian body, and Wagner that they arise from the early kidney segment or "urniere." Muus<sup>3</sup> describes six tumors to which he has had access, and discusses the origin of these growths. He believes that they occur as a result of some very early pathological process in the embryonic kidney, a certain portion of early developing kidney being thus retarded in growth; the rest of the structure developing along normal lines.

These tumors were early recognized, and seemed to have caused much confusion, being designated variously as "embryonic adenomyosarcoma," "embryonic adenoma," "sarcoma carcinomatosum," "adenosarcoma," etc. They occur for the most part in young children, one case having been reported, however, in a woman thirty-four years of age. The ages of the majority of the patients range from nine months to eight years. There is no difference in regard to sex.

The tumors, for the most part, are very large, smooth, or rather irregular or nodular, and are rather soft in consistence, especially when degenerative changes have taken place. On section they show a rather dense capsule, and the character of the cut surface varies in appearance corresponding to its constituent elements. Areas of softening and cysts are quite frequent. Where myxomatous tissue occurs the tumor has a soft, jelly-like consistence. According to Garceau, the growth arises in the parenchyma and does not infiltrate the kidney tissues as an ordinary malignant growth does, and it seldom involves the pelvis, the ureter, or the bloodvessels. The capsule of the tumor seldom ruptures, and the tumor is rarely adherent to the surrounding tissues. Extension into the renal veins may occur, and even direct invasion of the vena cava, but is not so common as in other malignant tumors. The tumors grow very rapidly, and may reach an enormous size in a very short time, in some cases filling almost the entire abdominal cavity. Weigert has described the only case of multiple mixed tumors, which occurred in the kidney of a stillborn child, and gave the appearance of atypical tubules of epithelium, growing principally between the kidney pyramids and ending in atypical glomeruli. Metastases are rather uncommon.

The tumors are composed of various tissue elements which usually are quite independent of each other. These elements grow with varying degrees of rapidity, the connective-tissue elements generally predominating. These tumors are composed of two or more of the following structures: epithelial cells lying either in tubular arrangement or in irregular masses or "pearls," which freely anastomose; connective-tissue cells, sarcoma-like in appearance, and of the round- or spindle-cell variety; myxomatous tissue; smooth and striated muscle; cartilage; bone; fat;

<sup>1</sup> *Berl. klin. Wchnsch.*, 1902, vol. xxxix.

<sup>2</sup> *Lectures on Surgical Pathology*, London, 1853.

<sup>3</sup> *Virchows Archiv*, 1899, vol. clv.

and two authors have mentioned a neuro-epithelial tissue. Connective tissue is the predominant feature, forming the framework in which the other tissues lie, and may so predominate as to lead to the diagnosis of pure sarcoma unless careful search is made from various parts of the tumor mass. Ribert states that there are no true sarcomas of the kidney occurring in children, but that all such cases should be regarded as mixed tumors. Smooth muscle tissue sometimes forms a large amount of the tumor substance, and is at times interwoven very closely with the connective tissue. The striated muscle is of less frequent occurrence than smooth muscle, but has been found in 25 per cent. of the cases studied by Walker and in 42 per cent. of those studied by Garceau.

The epithelial structures when present are of varying types. They may occur as tubular or glandular structures, the tubules being lined by epithelium of cuboidal type, and arranged in from one to three layers on a basement membrane. The tubules may form lobules separated by connective-tissue strands; at other times the epithelial cells lie in irregular groups or masses, which freely anastomose with one another.

**Symptoms.**—The presence of a tumor mass is the earliest symptom in the majority of these cases. These tumors lie in the affected area, show a very rapid growth, and sometimes attain a tremendous size. Hematuria is rather uncommon and only occurs probably when the mass invades the pelvis of the kidney, which is rather late and rare. The tendency of the tumors to remain encapsulated renders hematuria a rather unusual symptom. Pain is uncommon and occurs late in the disease, the symptoms mainly being referable to the pressure of the enlarging mass. Late in the disease emaciation and rapid loss of weight occur. The duration is usually less than a year.

**Diagnosis.**—A rapidly enlarging tumor mass in the kidney area with early emaciation and cachexia in a child is the symptom most characteristic in this disease. Hematuria occurs late and is infrequent. The methods of diagnosis are similar to those described under hypernephroma.

**Treatment.**—Early diagnosis and prompt surgical intervention offer the only hope of cure. The percentage of operative recoveries has much improved in recent years, but the outlook is gloomy, as recurrences have occurred in all but three of the operative cases noted.

**Benign Tumors.**—These include adenoma, angioma, lipoma, fibroma, and myxoma. The adenoma have been described. Angiomas are generally small and lie beneath the capsule. They may, however, vary in size from that of a pea to that of a walnut, and are occasionally seen in the medulla. Lipomas are also rare, and usually lie beneath the capsule. One case of lipoma the size of a child's head has been reported. Fibromas are usually minute and are found in the cortical portion, but are sometimes seen in the medullary portion.

**Symptoms.**—There are none unless the growth is large. Hematuria is very rare. Pain may occasionally be present, but is usually very slight, although it may be very severe if the tumor is large. In such cases symptoms produced by pressure may also be present. The *diagnosis* is usually made when the tumor is large and operation is generally indicated. Unless one can be certain as to the non-malignant character



of the disease, it is best to perform nephrectomy, although in certain cases partial nephrectomy may suffice to extirpate the tumor.

**Tumors of the Pelvis of the Kidney.**—These growths are very rare, more frequent in men than in women, and occur between the ages of forty and sixty. They are usually of two forms, a papillomatous and a flat, non-papillary form. The papillomatous forms are the more frequent and are very similar in character to the papillomas occurring in the bladder. Albarran has been able to collect 18 cases from the literature. In one case the papilloma grew down the ureter and subsequently invaded the bladder. Of the non-papillary forms, only 13 cases could be collected by Albarran. These are described for the most part as alveolar epithelioma. A squamous-cell carcinoma of the pelvis is exceedingly rare, one case having been described by Albrecht.<sup>1</sup> Although the histological character of some of these tumors of the pelvis is not malignant in appearance, they, however, are to be classed as malignant tumors. Stone in the pelvis of the kidney has been mentioned as an exciting cause of these growths. There is no definite symptomatology, hematuria, which is apt to be profuse, being about the only symptom present early in the disease. Attacks of pain from the passage of blood-clots are apt to occur, and in the papillary form pieces of tumor are occasionally, but rarely, found in the urine. The *diagnosis* is usually made as a result of surgical exploration. The *prognosis* is grave. In the nine cases reported by Garceau, recurrence followed in seven, either as distant metastases or in the scar of the wound. The *treatment* is excision—complete nephrectomy.

<sup>1</sup> *Arch. f. klin Chir.*, 1905, vol. lxxvii.

## CHAPTER XX

### URINARY LITHIASIS: RENAL AND URETERAL CALCULI

By HUGH HAMPTON YOUNG, M.D.

**Definition.**—Primary renal calculi may be defined as masses of urinary salts deposited in an amorphous or crystalline form in and about an organic nucleus and held together by an organic matrix. For the most part they presuppose a diathesis in which certain inorganic salts are supplied in excess to the kidneys for excretion; precipitation of such salts in the pyramids of Malpighi, consequent trauma to the tubular parenchyma in its attempt at elimination, and a urine in process of formation of a composition such as will find difficulty in dissolving out the precipitated salts and prove favorable to their further precipitation subsequently in the kidney itself, the renal pelvis or bladder. Certain inorganic calculi form by precipitation of salts into necrobiotic tissue.

**Classification.**<sup>1</sup>—Primary calculi are renal in origin, but the secondary calculi may form in any part of the urinary tract. We may distinguish calculi, according to the number, as the “solitary” and the “multiple,” and according to their position as renal, pelvic, ureteral, etc.

According to their composition they may be classified as: (1) The organic, of uric acid and its salts, calcium oxalate, cystin, xanthin, and urostealith. (2) The inorganic, consisting of the phosphates of lime and magnesium, and the carbonate of lime.

According to origin they may be classified hypothetically as:

1. “Of crystalline origin,” when they may be primarily resultant from irritation of the renal tubules by crystals.

2. “Of necrobiogenic origin,” when their first cause may be degenerated renal epithelium which invites calcification.

3. “Of microbic origin,” when their starting-point is infection of the urinary tract with urealytic microorganisms.

Secondary calculi, which are common to all dilatations of the urinary tract, may form in the renal parenchyma itself or in the renal pelvis, and thus come under the designation “renal calculus.” The conditions necessary for their formation are: (a) An infection of the living tissue, with a urealytic microorganism (*proteus bacillus*, certain *staphylococci*, etc.), with consequent inflammation, the freeing of ammonium carbonate and the appearance of pus in the urine, and (b) obstruction to the outflow of urine causing a stagnant pool in which a slimy mucoid matrix, composed of pus cells gelatinized by ammonia, may rest long enough to allow of sufficient infiltration with ammonium magnesium phosphate

<sup>1</sup> Léon Sourdille, La lithiase rénale primitive. *Arch. gén. de chir.*, September, 1907. Roy, La gravelle phosphatique primitive, *Thèse*, Paris, 1898.

to produce solidification. In pyonephrosis one finds this slime infiltrated with phosphates in every degree of consistency in freshly voided urine. The essential salt of this secondary calculus is ammonium magnesium phosphate, the formation of which in the urine is dependent on the addition of free ammonia to unite with the normal magnesium phosphate. Calcium phosphate and ammonium urate are also common constituents of this stone. The so-called "fusible calculus" is composed of ammonium magnesium phosphate and calcium phosphate. All phosphates tend to be friable in consistency and white to gray in color.

**Composition of Primary Calculi.**<sup>1</sup>—By far the most common are the mixed stones of urates and calcium oxalate in varying proportions and usually in layers in which one or the other salt predominates sufficiently to reveal on section more or less complete concentric rings. Frequently calcium phosphate and sometimes calcium carbonate or even cystin add a layer or more. Either the urates or oxalate may be lacking in these mixed stones, but they are most commonly associated. The phosphates and carbonate of lime are usually found together in the inorganic stones. Very rarely, if ever, do any of these salts form the sole constituent of a calculus. Should an ammoniacal infection supervene on these primary calculi they become invested with triple phosphates, and henceforth further growth is due to phosphates and carbonates alone.

If the outside primary layer of such a stone is composed of urates, a transitional ammonium urate layer intervenes between it and the phosphates, due to the ammonium of the urine combining with the uric acid of the primary calculus. Prout held that such a transitional layer of ammonium urates also occurred when a triple phosphate layer was enveloped by urates, but this must be a very uncommon occurrence.

In a report by Kahn and Rosenbloom<sup>2</sup> quantitative analyses of 25 renal calculi and vesical calculi are given, which show that true renal calculi are almost entirely composed of calcium salts. Their work confirms that of Rowlands and also that of Mackerell, Moore, and Thomas, who found that renal calculi were composed almost entirely of calcium oxalate; that uric acid is usually absent, and if present it is so only in very small traces; that phosphates are commonly present.

In most of Kahn's analyses calcium oxalate formed from 70 to 90 per cent., uric acid from 1 to 10 per cent. and phosphorus pentoxide 2 to 7 per cent. Some variations occurred, but not enough to disprove the fact that uric acid is of much less importance than calcium in renal calculi.

**Physical Characteristics.**—The physical characteristics of calculi vary greatly and are somewhat indicative of their composition. On these, rather than on chemical analyses, have been based many statements as to the nature of renal calculi. The so-called uric acid gravel is formed of fine reddish hard granules like cayenne pepper and sometimes of a size up to that of a pea. These are most commonly seen as precipitates in acid urine which has been standing for some time.

<sup>1</sup> The major portion of this section on the etiology and composition was written for me, after a laborious study of the literature, by Dr. George S. Gordon.

<sup>2</sup> *Jour. Amer. Med. Assoc.*, Dec. 21, 1912, p. 2252.



The hemp-seed gravel is similar, but of a dark gray or black color. Its chief constituent is calcium oxalate.

Phosphatic sand occurs in "alkalinuria" as white masses of amorphous calcium tribasic phosphates; or in cystitis as secondary white crystalline triple phosphate with an admixture of calcium phosphates and ammonium urate in a slimy mucoid matrix.

The most infrequent nearly pure calcium dibasic phosphate calculus is generally of the size of a small pea, cuboidal, with rounded edges and angles, grayish in color, smooth of surface, hard, and with a crystalline fracture. Multiple oxalates are very like these calcium dibasic phosphate calculi and are apt to be definite in composition.

The "mulberry stone" of calcium oxalate is tuberculated, stained blackish by altered blood, very hard, and of varying size up to that of a walnut or over.

The "pebble" of urates is of similar dimensions, oval, of sandy surface, medium hardness, and grayish to reddish from admixture with urinary coloring matters.

"Staghorns," or "coral calculi," are of the same materials, *i. e.*, urates (Osler), color, consistence, and surface appearance, but of size and shape like a mould of the renal pelvis.

The "jackstone" calculus, of brownish to blackish color and hardest consistency, is another form of oxalate (Fowler<sup>1</sup>).

The *xanthin* calculi are "of a pale yellow color and exhibit a waxy lustre when rubbed" (Adami<sup>2</sup>). They vary in size from a pea to a hen's egg. A *cystin* calculus is hard, oval, light amber, glistening of surface, rough and granular but non-crystalline, and resembling small masses of amber stuck together without definite arrangement (Fowler).

Urostealiths are "in the moist state soft and elastic at the temperature of the body, but in the dry state they are brittle, with an amorphous fracture and waxy appearance" (Hammarsten<sup>3</sup>).

Calcium carbonate calculi "have mostly chalky properties and are ordinarily white" (Hammarsten). "Naunyn differentiates two forms in man, the one brown and spicular, the other pale and smooth, but of relatively great hardness" (Adami).

**Nucleus.**—This is usually a solidified agglomeration of the same salts of which the calculi are composed, and forms the core. It differs from sediment inasmuch as it has a colloid matrix, and on the other hand from stone in not being laminated. It originates in the renal tubule, which is the only part of the urinary tract of small enough calibre to retain so small a body. As it increases in size it erodes the renal tissue, and if this takes place toward the renal pelvis it frees itself ultimately into a calyx, where it may unite with other similar nuclear forming material and become gravel or stone, pass on to lodge in the renal pelvis or other portions of the urinary tract, or be voided in the urine.

Esbach<sup>4</sup> says that a primary phosphatic nucleus is always replaced

<sup>1</sup> *Johns Hopkins Hospital Reports*, 1906. vol. xiii.

<sup>2</sup> *The Principles of Pathology*, 1908, vol. i.

<sup>3</sup> *Physiological Chemistry*, 1908.

<sup>4</sup> *Les Calculs Urinaires*, Paris, 1885.

by oxalates or urates if they afterward envelop it. Tuffier<sup>1</sup> has demonstrated experimentally that foreign bodies, unless they can supply an organic material for urinary contents to lodge in, do not form nuclei. Bilharzia eggs were said by Fagge to form the nuclei of uratic calculi in Egypt. Blood-clots sometimes form the core of a stone. Fullerton, basing his opinion on the analysis of seven calculi, holds that bacterial agglomerations do not form nuclei. Inorganic calculi usually lack a nucleus, unless formed about a foreign body.

**Size.**—The size varies from that of fine gravel to the limit imposed by their enveloping-tissue bed. As the result of abnormal back pressure due to interference with the outflow of urine or to erosion of tissue by the growing calculus, a stone may be even larger than any normal expansion of the urinary tract.

**Form.**—The forms assumed are dependent on their composition, the shape of their nucleus or nuclei, pressure from contiguous stones (in which case they become faceted), the conformation of the tissue bed in which they form, and on the way the urinary stream impinges on their surfaces to add fresh laminae or erode, according to whether the urinary contents favor growth or disintegration.

**Color.**—Calculi are composed of colorless crystals and matrix. Their varying tints come from the urinary pigment, uroerythrin (Adami), or from blood-pigment, and vary as these vary in affinity or amount in the urine. When urates form, urinary pigments are much more in evidence in the urine than when phosphates or cystin calculi form, and consequently are more apt to be colored. Oxalates, if of coarse surface, erode into the vascular layer of the urinary tract, and blood-pigment stains them. Smooth oxalates are whitish. Cystin calculi may change color on exposure to the air, probably because they contain urobilinogen.

**Number.**—Probably no calculus forms from a single salt-impregnated renal cast, but about an agglomeration of such. Multiplicity depends on the coalescing of such infarcts either in situ by erosion into neighboring tubules or after expulsion into a calyx. The adhesiveness of the mucoid matrix would vary with the amount of salts it contains, and if it is saturated it tends to form the nucleus of a stone by itself; while if it is in a more glutinous condition and comes in contact with similar infarcts fusion would occur. In the first instance multiple stones would form, and in the second a single calculus. If this hypothesis be correct there would hardly be a limit to the number of calculi forming in a kidney, and such is the case. On the other hand, many of these nuclei would escape in the urine before attaining size enough to prevent their exit.

**Bilaterality.**—Holt,<sup>2</sup> after 1000 autopsies on infants, states that granular deposits are generally seen in both kidneys. Legueu<sup>3</sup> holds that in half of the cases where calculi form in one kidney the other is similarly affected. Albarran<sup>4</sup> considers the frequency of stone on both sides as an argument in favor of the systemic origin of calculus.

<sup>1</sup> *Étude sur la chirurgie du Rein*, 1889.

<sup>2</sup> *Diseases of Infancy and Childhood*.

<sup>3</sup> *Les calculs du rein et de l'uretère, Thèse*, Paris, 1891.

<sup>4</sup> *Lancet*, 1892, vol. i, pp. 1345, 1339.

**Disintegration of Calculi.**—Adami, speaking of uric acid stones, says: "The evidence seems to be conclusive that through keeping the urine alkaline through long periods by giving sodium bicarbonate, alkaline soaps, etc., not merely is gravel arrested but the stones within the bladder after such treatment show clear evidence of erosion."

**Etiology.—Age.**—Calculi are found in the kidney throughout life, but are very rare in old age. Fry and Martin,<sup>1</sup> in a study of 100 hospital infants under the age of three months, found an abundance of uric acid in the voided urine of 26 of them, of whom 19 died, and in 7 of these autopsies were done which demonstrated uric acid infarcts in the apices of the pyramids. Holt says, basing his remarks on 1000 autopsies, that "small renal calculi are very common in infancy," but they are usually voided during the first two years of life. He found one large renal calculus. By far the greater number of clinicians hold that renal calculus is rare in early life, but in the light of these figures they are evidently at fault. Calculi in the kidneys are most in evidence about the fourth decade. To this period belong the urate infarcts of the gouty and the calcium oxalate stone. Osler refers to the calcium phosphate infarcts of old age. Old people are not so prone to stone in the kidneys, because a "crystalline diathesis" declares itself, if at all, before this period, and the patient has passed all his calculi (at least as far as the bladder), had them removed by operation, or has a ureter sufficiently dilated, by the previous passage of stone, to offer no obstruction to the passage of calculi to the bladder.

**Sex.**—That renal calculi occur more frequently in men than in women is generally accepted, but there do not appear to be statistics showing the relative frequency. Small renal calculi which pass into the female bladder are easily voided, but the same anatomical structures tend to hold them in the kidney in the female as in the male.

**Heredity.**—Hereditary predisposition, the "péché original" of D'Etiolles, is almost universally admitted, and many authorities hold that urate gravel ranks as an evidence of gout. Oxalates and xanthin are so closely related to urates that they may be fathered by the same etiological factors. Cystinuria and a tendency to form cystin calculi also "run in families."

**Occupation.**—"Sedentary occupations seem to predispose to stone" (Osler). D'Etiolles held that exercise was the "bellows blowing" which gave a good intake of oxygen through the lungs and thus secured combustion of tissue waste, and statistics and observation bear out the theory that stone formation is generally dependent on occupation only so far as the occupation is an active or sedentary one. Those engaged in plumbing and who use alcohol in excess are predisposed to renal calculi as to gout. Hutchinson called attention to the freedom of sailors from stone and attributed it to their salt diet, but D'Etiolles states that naval officers, notwithstanding they ate an excess of salted food in his day, were as prone to calculi as others. Civiale's list<sup>2</sup> of prominent men, "victims of the sharp and craggy stone that cruelly pricks and

<sup>1</sup> *Trans. Amer. Pediat. Soc.*, 1903, p. 150.

<sup>2</sup> *Traité de l'affection calculieuse*, Paris, 1838.



tears," includes, among others, Cromwell, Bacon, Boerhaave, Louis XIV, George IV, Napoleon I, Peter the Great, Montaigne, Newton, Horace Walpole, Fothergill, Hartley, Harvey, Mascagni, and Scarpa.

**Diet.**—How absolutely unestablished is the etiology of calculi could be no better demonstrated than by noting the discord of deductions drawn by eminent authorities in the attempt to incriminate diet as causative. Cadge and Dickinson held that hard drinking-water was the cause of stone in Norfolk. Denny thought absence of lime in drinking-water caused stone in Holland. A. E. Roberts holds that stone in India is uncommon among those natives whose food contains sodium chloride, and Hutchinson believed that sailors were exempt from stone because of their salt diet. Yet Morris says that "salted meats are inductive of renal concretions," and D'Etiolles held that naval officers, who in his day ate much salt food, were especially subject to stone. Many maintain that ingested oxalic acid is a cause of oxalate calculi, yet Chabrié lived on food rich in oxalates for a month and did not succeed in finding oxalates in his urine.

If the theory so well put by Fitcher, "that owing to some organ or organs failing to produce a ferment (which normally is necessary for the proper destruction or oxidation of uric acid) oxidation of uric acid does not occur, and consequently accumulates in the blood in excess," is correct, then the ingestion of food rich in nucleins would cause an excess of uric acid and possibly xanthin to be presented to the kidney tubules for excretion; and this is a prime step in calculus formation. Exclusion from the diet of nucleins would cut off this supply of material.

There is now a consensus of opinion (Guyon, quoting Chabrié, excepted) that ingested oxalic acid appears, at least in part, unchanged in the urine. It does not seem improbable that, as demonstrated by Dickinson and Roy, the drinking of lime-water furnishes one of the bases for inorganic calculi.

**Distribution.**—Stone is common in the cold as in the warm climates, in the moist as in the dry, in the highlands as in the lowlands, inland as well as in countries bordering on the sea. It is common in Iceland. There are "stone districts" in England (Norfolk, Bristol, etc.), the west of France, about Moscow in Russia, some parts of Germany, in lower Egypt, in the uplands of India, and in Holland. In America stone is fairly evenly distributed and favors no particular locality. Norway, Sweden, and Styria were said by Roberts in 1866 to be practically free of stone. It is very common in India and China.

**Previous Diseases.**—Almost every form of disease is referred to by authorities as causative of renal calculi, and it would be strange indeed if each of them had not been at one time or another the precursor of stone. Their etiological relation is not at all proved except in the following ailments, whose rôle has been more or less fully substantiated:

1. Those diseases which interfere with the complete combustion of food or tissue waste into urea and permit of the circulation in the blood of an excess of uric acid, oxalic acid, xanthin, or cystin. These tend to form organic stones in the kidney. Such diseases are: (a) Intestinal

disorders which allow the toxic mid-products of mucosal enzyme digestion, such as albumoses, etc., to reach the liver and by affecting it produce "hepatic incontinence." (b) All liver diseases which interfere with its urea-forming function; especially to be noted is hepatic cirrhosis. (c) Lung disease which limits the intake of oxygen. (d) Cardiac and arterial diseases (whether or not produced by alcohol or lead), which do not allow of sufficiently free circulation to permit the blood to be well oxygenated. (e) Gout. (f) Diseases which may supply an excess of uric acid to the kidney without the necessity of its passing through the liver, such as leukemia.

2. Ailments which produce a fatty degeneration of the renal tubular epithelium, such as (a) the above diseases, which are accompanied by crystalline deposits in the kidney causing fatty degeneration, (b) fevers and (c) obesity.

3. Fagge attributed part of the frequency of stone in Egypt and Natal to Bilharzia eggs in the urinary tract, which provide a nucleus.

4. Disease characterized by renal hemorrhage, such as hemophilia and tuberculosis. The blood-clot acts as a nucleus.

5. Oxaluria has been found in certain forms of dyspepsia of a somewhat neurotic type, in confirmed obesity and in diabetes (Adami).

6. "Alkalinuria" is due "first to a diet which raises the alkalinity of the blood, as a vegetable one, in gastric diseases with considerable loss of hydrochloric acid to the body through hypersecretion with motor insufficiency and vomiting or lavage, perhaps diarrhœa also, and specially as a symptom of neurasthenia (Peyer), without any of the above-mentioned causes. In such a case during a period of neurasthenia a diminution in the phosphoric acid to about half and an increased calcium output have been found. The nitrogen was also decreased. It seems to be excessive calcium, relative to phosphoric acid, which leads to precipitation. It occurs in persons also after sexual excesses and in the depression following psychical exaltation, in which case the cause is not known, but a nervous control suspected. It is often found among mental cases (Heinicke)" (Emerson).

Fullerton states that microörganisms do not form the nucleus of stone, although they may be present in the layers surrounding it. Thus it would seem that the bacilluria which so often accompanies and follows typhoid fever for so long a period is not specially likely to favor calculus. Secondary calculi of ammonium magnesium phosphate and other secondary salts follow local infection, such as is specially liable to supervene on spinal paralysis.

Is it necessary to go farther than the "urinary functions" to determine the cause of gravel? In other words, can the kidney act independently of other glands and tissues and elaborate material for stone without regard to what abnormal or normal metabolism provides for it? We think it cannot. Sufficiently pertinent facts are known to indicate that no gland or tissue acts independently of other tissues even in disease. Moreover, excretory glands to functionate properly depend on other tissue to put proper end products of metabolism into the blood-stream.

1. **Urinary Reaction.**—In its relation to the formation of calculi:

L. Lickwitz<sup>1</sup> states that uric acid and its salts have a high concentration in the urine in spite of the sodium ions present. (Salts of sodium diminish and albumin increases the solubility.) This is explained by the colloidal structure which he attributes to the urine. The formation of a sediment depends more or less on its colloidal substances. Evidently acidity exerts an influence. These colloids are responsible for the high uric acid and urate content of the urine. The reaction of the urine does not affect calcium oxalate as shown by its insolubility in strong mineral acids. He illustrates the importance of these colloidal substances by two experiments. In the first, he extracted with ether a colloidal substance from urine. The phosphates precipitated rapidly after this removal. The second experiment was performed by dialyzing urine in the presence of water, the urinary salts being crystalloids dialyze and precipitate easily in the aqueous solution. The precipitate most often is composed of calcium oxalate.

2. **Crystallization.**—As the forms of crystals may have to do with the production of matrix material, the more spiculated being more irritating would produce more tissue degeneration, and thus perhaps more irregularly shaped nuclei. Once embedded in their matrix their forms are modified, as shown by Orde, and probably no longer have to do with the general outlines of calculi, only inasmuch as they may or may not supersaturate a nucleus to such an extent that it will not adhere to other nuclei.

3. **Origin of Uric Acid.**—All the uric acid which passes through the liver is normally converted into urea by a uricolytic enzyme, but about half of the endogenous uric acid escapes the liver, and this is excreted normally unchanged by the kidneys. It amounts to approximately 0.7 gram per day. When in excess it deposits in the renal pyramids as amorphous or crystalline bodies like tophi in the ear or chalk stones. Excess of uric acid supplied to the kidney for excretion may be due to: (1) Failure of the liver to produce sufficient uricolytic enzyme to transform uric acid into urea, or (2) excessive formation of endogenous uric acid which can short-circuit the liver, as it were, in reaching the kidney.

It does not seem likely that the liver is solely at fault in these diatheses although it is held that the kidney is "more sinned against than sinning" when stones form. The fault may be one mainly of the liver, still the liver in its turn may have its handicap thrust upon it by gastro-intestinal disturbance, diseases of the lungs, leukemia, anemia, cardiac disease, etc. Moreover, other tissues than the liver may be responsible for combustion of waste products and their default be the main cause of calculus formation, but this seems very unlikely. In leukemia the uric acid from the nucleins may reach the kidney in very considerable quantities unaffected by the liver metabolism.

**Origin of Xanthin.**—Another of the mid-products of metabolism which furnishes the salts for renal calculi is xanthin. This is merely uric acid less one atom of oxygen, and that it is so very rarely found in the urine would indicate that it is almost always oxygenated, at least to uric acid, in the body. Still there may be a very small amount of it in normal

<sup>1</sup> Abstracted in *Journal de D'Urologie*, November 15, 1913.



urine. Its excess would be due to the lack of an oxydase, probably of the liver, or to excessive endogenous formation.

**Origin of Oxalic Acid,  $C_2H_2O_4$ .**—Chemically, Simon says, "oxalic acid may be regarded as a complete oxidation product of uric acid." Oxalate calculi are so often mixed with urates as to indicate a close relation etiologically, and clinicians, in speaking of causation, have very often drawn no distinction between the two. Like uric acid, it may be exogenous or endogenous, and "is increased in various diseases in which the oxidation processes are manifestly at fault." On the other hand, pure oxalic calculi, if they exist, would demonstrate that the "oxalic diathesis," recognized by Adami, is independent of "uric acid diathesis." On the other hand, authorities recognize indigestion in neurasthenia as causative of oxaluria; oxalic calculi do not dissolve in alkaline urine; they often have a layer or more of calcium for their base, all of which would seem to indicate some relation to the "alkalinuria" diathesis.

**Origin of Cystin,  $C_6H_2N_2S_2O_4$ .**—This salt, so uncommon in urine and the calculi of which are so rare, has been the subject of much controversy and research. Fowler, after passing under review the various theories of its origin, concludes: "Cystinuria, or the presence of cystin in the urine, is, therefore, to be looked upon as an indication of defective proteid metabolism. . . . It is not known in what part of the body cystin is formed, but the suggestion was made long ago that the liver is responsible. We have seen that the recent work of Friedmann lends some support to this view. It remains, however, for further clinical and experimental work to solve the question."

**Origin of Calcium and Magnesium Phosphates and Calcium Carbonates.**—These salts escape through the urinary tubules as sediment in what Emerson calls "alkalinuria" (the commonly but falsely so-called "phosphaturia"), a condition in which "we are dealing with a diminished acidity, and it seems with a diminished excretion of phosphoric acid and an increased elimination of lime" (Hammarsten). "Recent study of these cases with symptoms of neurasthenia and a phosphatic sediment in the fresh urine would indicate an abnormality in the calcium metabolism—an absolute increase of this with a decrease of phosphoric acid" (Osler). These, however, are the amorphous phosphates, and do not tend to form calculi except secondarily to an aseptic necrosis. In the "phosphatic diabetes" of Tessier, on the other hand, calcium salts never precipitate in the urine. These amorphous phosphates, the crystalline calcium phosphate, calcium carbonate, magnesium phosphate (amorphous), magnesium phosphate (crystalline), are normally present in the circulation in some form and may deposit in necrobiotic cellular tissue to form the non-nucleated, non-laminated, pure phosphate stone so-called, or layers on an oxalate or other organic calculus. No diathesis to increase the amount of lime in the organism is necessary to explain this. The process is very similar to the calcification of a tuberculous focus. On the other hand, if there be a phosphate and carbonate diathesis in which these salts in a crystalline form are furnished to the kidneys in excess resulting in degeneration of the renal epithelium, inorganic stone may have the same genesis attributed to organic calculi.

4. **Origin of the Matrix for Organic Calculi.**—(Urates, oxalates, cystin, and xanthin.) Rainey is said to have been the first, in 1858, to call attention to the effects of colloids on crystallization. Orde's experiment of crystallizing calcium oxalates in gelatin demonstrated that salts take on bizarre shapes or become amorphous under such conditions. Tuffier found that an aseptic foreign body placed in the renal pelvis of a dog became in time merely frosted with urates and phosphates, and that there was no agglomeration of salts. The colloid cement to hold the crystals together was wanting. "Poisoning with oxalic acid (Kobert, Kusner, and Newberger) leads to abundant deposits within the kidney of calcium oxalates" (Adami). Ebstein and Nicolaier fed dogs on amide of oxalic acid, and at autopsy they demonstrated not only oxalate of lime in the tubules, but also fatty degeneration of the epithelium. Sourdille says, "The elimination of crystals in the interior of secreting tubules does not take place without wounding the tubules." This is "néphrite lithogène"—a nephritis set up by the crystals which produce a colloid material for organic stone as distinguished from "néphrite lithiasique" or a nephritis the result of calculus in the kidney. Strictly speaking, both forms are due to stone, but in the former only crystals are present to cause nephritis.

**Origin of Matrix for Inorganic Primary Calculi.**—(Calcium carbonate and calcium and magnesium phosphate.) Litten, in 1881, tied the renal artery, and necrobiosis of the epithelium of the renal tubules followed, which formed the matrix for deposition of calcium salts. Dupré found necrosis in the renal epithelium in infants who had been poisoned by Spanish-fly blisters, and calculus followed. The writer has seen a microscopic section of the kidney of a man poisoned with corrosive sublimate which shows the renal tubules stripped of their lining cells and filled with granular deposits, presumably of lime, embedded therein. "Klotz showed that if celloidin capsules filled with fat or a fatty acid be inserted into the peritoneal cavity of a rabbit, in the course of a few days these are found to contain an amount of calcium far in excess of that present in the body fluids of the animal" (Adami). One can hardly avoid the conclusion that intoxication by ingested poison or by disease which would be severe enough to cause necrosis of the renal tubular epithelium would furnish a matrix for calcium and magnesium salts to precipitate in. But some of these salts are also crystalline, and as such, owing to an alkaline diathesis if supplied in excess to the kidneys for excretion, may be capable of setting up a lithogenous nephritis similar to that induced by the organic crystals.

Ohlmacher<sup>1</sup> thinks that bacterial infection plays an important rôle in the formation of renal calculi. He quotes 4 cases of Wright in which staphylococci were found, and gives details of seven cases, in 4 of which the staphylococcus, and in 3 the colon bacillus was found. The 4 staphylococcus cases all had typical attacks of renal colic, but the colon infections were less typical. In only 1 case was operation performed (vesical calculus). In the other cases the author claims a cure (or relief of all symptoms) by injections of autogenous vaccines.

<sup>1</sup> *Jour. Amer. Med. Assoc.*, April 19, 1913, p. 1213.

5. **Sediment, Gravel and Stone.**—When these salts are washed out of the tubules of the kidney, why do they at one time form urinary sediments, at another gravel, and at another stone? The salts which are excreted as sediment in the fresh urine are, for the most part, amorphous and consequently not so irritating to the renal epithelium as to induce inflammation, with a resultant colloid into which the particles of salt may precipitate. These may continue for years without the formation of true gravel or stone.

6. **Formation of Calculi.**—Fluid flows through the tubules, dissolves the solids in the tubules, and is in part absorbed; what is left leaves the tubule as the finished product—urine—which thence flows through calices, renal pelvis, etc. Now, if it can dissolve out the salts in the tubular epithelium, but owing to absorption not hold them in solution, and they are amorphous urates or phosphates, it carries them as sediment with probably little or no irritation to any part of the urinary tract. If the salts are crystalline and sufficiently infiltrate their matrix, they may occlude a tubule or more at first, but ultimately be washed out entire or in an agglutinated mass of similar plugs from other tubules forming gravel. Yet again these crystals, forming infarcts, may erode their containing tubule and cement themselves to similar infarcts in neighboring tubules in the kidney itself, may then erode into the calyx, and again form gravel.

They may be retained in the renal tissue still longer and erode into tubules with patent lumina, through which fresh salts may be added to their composition. They may erode in one place into a calyx, yet not free themselves from their kidney bed, and increase in size on the renal pelvic side by deposition from the supersaturated urine, passing their outcropping into the calyx. They may free themselves into a calyx as a nucleus so large as to be voided only with colic or remain to become laminated because of the changing nature of the urine contents in which they are bathed. Once the nucleus is of size to be retained it will be bathed by the products of renal inflammation until the renal cells recover. Thus a matrix for whatever salts may be precipitable in the urine is furnished to supply fresh layers on the calculus. Stones may remain embedded in the kidney for their entire period of existence, but considering that they form in the renal pyramids and have the pressure of urine behind them and the power of necrosis by pressure in front, it is little wonder that they practically always slough out into the calyx, thence to be voided or remain for increasing growth in the calyx, pelvis of the kidney, ureter, bladder, or prostatic urethra.

**Pathology.—Lesions of the Kidney and Ureter.**—When the calculus is aseptic the kidney may remain fairly healthy, and there may be no inflammatory complications. Albarran claims that every calculous kidney, although it may appear normal, presents lesions of nephritis. He thinks these alterations are of etiological relation, but, also, that when the calculus is formed the lesions become aggravated as a result of the elimination of salts. This form of nephritis is diffuse, beginning by epithelial lesions, which are soon accompanied by interstitial sclerosis. In the more advanced periods the kidney is retracted and becomes



nodular. The capsule becomes adherent, and numerous small cysts are seen. In certain cases, according to Albarran, the kidney is very large and studded with cysts of various sizes, resembling a polycystic kidney. If the calculus obstructs the ureter more or less completely, *hydronephrosis* develops. This may be associated with marked dilatation of the pelvis and calices, with great thinning of the renal cortex. It has been shown that intermittent and incomplete stoppage of the ureter with a calculus is much more apt to lead to hydronephrosis than a complete blocking. In one of the writer's cases, in which the ureter was completely blocked and five calculi were present, the kidney was markedly contracted and atrophic, forming in reality a fibrous capsule for the calculi. There was apparently no secreting substance left, and no fluid secreted. In some of these cases of contracted kidney the perirenal fat becomes greatly increased, forming a large, fat, tumor-like mass around the kidney. Renal calculi may remain for years without any accompanying bacterial infection, but it is more common to find bacteria present, and they may easily precede or follow a lithiasis. In some cases this infection is of a mild degree, and accompanied only by a slight chronic inflammation of the pelvis and a certain amount of nephritis. In other cases numerous small focal areas of infection are present in the renal substance, and pyelonephritis exists.

When the inflammation becomes severe, with extensive abscess of the pelvis of the kidney, *pyonephrosis* usually results, often associated with great thickening or complete destruction of the cortex and the formation of a large, irregular fluctuating mass. At times the cystic distension involves only a portion of the kidney. This happens particularly in cases in which the renal pelvis is of unusual type, viz., those cases of multiple pelvis or with two or more ureters. In one of the writer's cases there was a large pyonephritic abscess of the upper half of the left kidney, the lower half of the kidney being normal and emptied by a separate branch of the ureter, which joined the other branch about seven inches below the kidney. The cystic distension of the kidney may reach an enormous size. There is often considerable perinephritis, and in some cases the capsule becomes greatly thickened and very fibrous.

**Number.**—The number of stones may vary greatly. In 48 cases operated on by Israel, there were 26 with more than one calculus, the largest number being 36 in one kidney. From one of the writer's patients thirty-four stones were removed from the right kidney and fourteen from the left six weeks later. According to Israel both kidneys are the site of stone in 27 per cent. of the cases, and according to Legueu in 50 per cent. According to the writer's experience these figures are too high.

**Location.**—Calculi are most frequently in the pelvis or in one or more calices. At times they may be embedded in the substance of the kidney, and at others have passed beyond the pelvis into the ureter, in which there are three points at which calculi most commonly lodge. These places are points of natural constriction of the ureter, and lie (1) just below the beginning of the ureter, (2) just at the crossing of the iliac vessels, and (3) in the terminal portion of the ureter. A calculus which has escaped from one of the calices or pelvis into the ureter may stop

at any one of these points, or it may pass into the bladder and remain there as a vesical calculus. Not infrequently these are caught at the ureteral orifice, where they produce a fusiform-like swelling or project into the bladder.

**Symptoms.**—The symptoms of renal calculus are very variable. In those cases which are associated simply with the passage of sand there may be no symptoms at all, but more often there is a feeling of discomfort in the back or region of the kidney, which is relieved by its passage. Not infrequently, however, this sand produces an irritation in the ureter, bladder, and urethra during the passage. When a definite calculus has been formed the symptomatology depends considerably on its location and its movements. Not infrequently there are no subjective symptoms produced, and in one case the disease was present for a period of many years, and the only symptom which attracted the patient's attention was a recent onset of fever followed by pyuria. Yet in this case fourteen large calculi, some considerably larger than a hen's egg, were present. In another case a calculus remained in the ureter for ten years without symptoms after the first attack of colic.

In a study of twenty-one cases there was a history of *pain* in 17, and in 13 cases it was of a colicky character, radiating toward the groin and generally into the testicle. Only one was described as radiating to the end of the penis, and in this case several calculi were passed per urethra. The pain is most commonly described as that of a dull, aching character, located in the small of the back on the affected side and sometimes beneath the ribs in front. This pain is generally increased by active exercise, by riding on horseback or in a rough vehicle, and by stooping forward. Most often it is slight in character, although more or less continuous. In a few cases, however, it is severe, and occasionally is present also on the other side of the back. The presence of a reno-renal reflex (*i. e.*, pain referred to a sound kidney from a diseased kidney in which there is no pain) has now been recognized in a sufficient number of cases to warrant the acceptance of this as a rare but definite occurrence. This remarkable symptom must be carefully borne in mind. An apparently clear history of calculus is not, therefore, sufficient to decide as to the kidney involved; the wrong kidney has been operated upon in quite a number of cases. The character of the calculus has much to do with the severity of the pain and the traumatism produced, according to Osgood, who says that a sharp, rough calculus the size of a pinhead may produce the most agonizing colic, while a smooth stone nearly as large as a cherry may remain in the pelvis or ureter throughout life without severe pain. Calculus in the kidney or in a calyx may produce a pain referred all along the ureter, and a calculus impacted in the lower end of the ureter may produce typical colic in the region of the kidney.

*Renal colic*, which is the most characteristic and most distressing symptom of calculus, fortunately occurs at more or less prolonged intervals. It is frequently ushered in by vomiting, which is soon followed by pain of extreme violence in the lumbar region of the affected side, usually associated with muscle spasm, which causes the patient to double up and frequently to get on his hands and knees. Radiation

of the pain from the lumbar region along the side downward and inward toward the groin and into the scrotum and testicle occurs, causing marked retraction of the latter. The course of this pain is usually supposed to follow the genitocrural nerve. In some cases it extends also down the ureter into the bladder, and is associated with vesical irritability and frequency of urination; but usually this is rare, except when the calculus has passed to the lower portion of the ureter or into the bladder. An attack of colic may be associated with great systemic depression, chills, fever, rapid pulse, pallor, and severe gastro-intestinal disturbance, and not infrequently persists in its intensity for several hours, until it has been relieved by the use of large doses of morphine. Not infrequently several injections of morphine are necessary to obtain relief, and it is a noteworthy fact that the patient is able to withstand much larger doses during these attacks than at other times. Fortunately, nephritic colic is apt to disappear after the first attack and not to recur for several months, although occasionally it may recur for several successive days and cause great prostration. During or after the attack the urine usually contains a certain number of red-blood cells, and occasionally leukocytes; but in some cases both of these may be absent. The cessation of the colic is sometimes due to the successful passage of the calculus into the ureter, and occasionally into the bladder, but most often no calculus is passed, and the cessation of the attack must be attributed to a change in position of a calculus—a stone which has become engaged in the upper end of the ureter may in some way become misplaced.

In this series of 21 cases, colic was present at one time or another in 13, but in only 7 cases was there a history of the passage of a calculus into the bladder and out through the urethra. Owing to the fact that small calculi may not be observed, these figures may be erroneous.

Renal colic is not, however, absolutely diagnostic of stone. It occurs with other diseases in which the ureter suddenly becomes blocked, either by a blood-clot, a fragment of tumor, a mass of muco-pus, or torsion of the renal pedicle. It is also simulated very closely in certain cases of chronic prostatitis and seminal vesiculitis. Hematuria is also a variable symptom. In some cases it is more or less continually present, and in others it is never present macroscopically. In the 21 cases it was present at one time or another in only 8, according to the statement of the patient. When infection and inflammation occur secondarily to calculus, and the pus formation is considerable, hematuria is less apt to occur, in the writer's experience, and often the attacks of colicky pain disappear. The presence of a swelling noticeable to the patient is rare, and occurred in only 3 of these cases. Gastro-intestinal disturbances are fairly common according to some authors, but were present in only 5 of this series. Digestive disturbances are most apt to indicate uremia and should lead to a very careful study of the renal function.

*Anuria* is one of the most alarming and serious symptoms which occasionally occur with nephrolithiasis. Watson, who has made a careful study of this subject, lays down the underlying causes as follows: (1) The simultaneous blocking of the ureters of both kidneys; (2) the blocking of the ureter of one kidney, the other kidney being functionally incapable;



(3) the blocking of the common stem of the two ureters when they are fused, or of the single ureter of a fused kidney; (4) the blocking of the ureter of one kidney and the lessening of the function of the other by reflex influence, the latter organ being normal or but moderately diseased. Calculous anuria is one of the most fatal complications of the disease, as shown by the fact that in 110 cases treated expectantly there were 80 deaths, a mortality of 72 per cent., and in 95 cases treated by operation there were 44 deaths, a mortality of 46 per cent.

Vesical irritability may, according to Watson, Desnos, and others, be the only sign of renal calculus. In the writer's case vesical symptoms were present in only 6 of the 21 cases, and in very few of these was this more than a slight irritation. Apparently the bladder is usually free from irritation, unless a calculus has passed through the ureter or has become lodged in its lower end, in the juxtavesical, intramural, and intravesical portions of the ureter. In the *Transactions of the American Association of Genito-urinary Surgeons* for 1907 the writer reported 7 cases of calculus lodged in the lower portion of the ureter—2 intravesical, 3 intramural, and 2 juxtavesical—and the following conclusions were drawn: When the stone is situated in the ureter just above the bladder the symptoms are pain in the pelvis, sometimes radiating to the penis, but not associated with increased frequency of urination, with pain in the rectum or on ejaculation. Intermittent renal colic occurs, and perhaps pain in the testicle. When the stone is situated in the intramural portion of the ureter and does not project into the cavity of the bladder, there may or may not be frequency of urination; but there is always a pain radiating into the penis at the end of urination, and there is generally pain on ejaculation, either during intercourse or with nocturnal emissions. In one of the three cases there was also pain in the rectum. Intermittent attacks of renal colic also occurred in these cases. When the stone is caught in the ureteral orifice and projects into the bladder the symptoms are more severe than in other locations, and present a remarkable and typical symptom complex of pain, renal, vesical, rectal, seminal, and testicular in character. In one of the cases with this syndrome, the patient complained of a frequent desire to urinate, pain in the bladder, radiating to the glans penis at the end of urination, a constant severe pain in the rectum, which was worse on defecation, a severe pain during sexual intercourse, which came on at the moment of ejaculation, and intermittent attacks of pain in the left kidney and testicle. Examination showed a calculus about 1 cm. in diameter projecting partly into the bladder through the ureteral orifice. All of these symptoms disappeared after removal of the calculus. The explanation of this combination of symptoms is evident as soon as we remember the intimate association of the lower end of the ureter, the seminal vesicles, the rectum, and the bladder.

**Diagnosis.**—The examination should include a thorough study of the patient, including careful physical examination, urinalysis, cystoscopy, ureter catheterization, radiography, functional diagnosis of the kidneys, etc. Abdominal examination is unfortunately often very unsatisfactory. In many cases nothing can be made out in the region of either kidney,

and in others there is only a slight tenderness. In only 13 of the 21 cases seen by the writer was any abnormality noted in the region of either kidney, and in only a few of the cases was there marked enlargement. Tenderness is supposed to be a very suggestive sign of calculus, but it is very frequently absent. When the kidney is enlarged it is often difficult to differentiate between nephrolithiasis with pyonephrosis and renal tumor. The presence of pus in the urine is more common with calculus, but is also seen in tumor. Careful urinalysis, with estimation of urea, total solids, and the determination of the functional state of the kidneys is important. When the phthalein excretion is low cryoscopy of the blood or preferably determination of the blood-urea should be performed. Before operation is attempted it is important to know the condition of the "other" kidney. The radiograph is of great certainty, and almost all renal and ureteral calculi can be demonstrated in this way. The pure uric acid calculus is the most difficult to detect, and some competent radiographers claim that it cannot be shown. In suspected cases the passing of a wax-tipped catheter will almost invariably furnish evidence if a stone is present. The most deceptive shadows are those shown by phleboliths, which not infrequently occur in the pelvis adjacent to the lower portions of the ureter. The diagnosis is made all the more difficult owing to the fact that phleboliths are not infrequently associated with pain. In such cases a positive diagnosis can usually be made by taking an *x*-ray photograph with a stiletted catheter in the ureter, or by outlining the course of the ureter with an injection of collargol.

**Differential Diagnosis.**—The more common diseases which are to be considered are tumor of the kidney or ureter; tuberculosis; essential renal hematuria; stricture or torsion of the ureter, with hydronephrosis; vesical disease, such as stone, tuberculosis or tumor; prostatic hypertrophy and carcinoma; chronic prostatitis; seminal vesiculitis. Disease of the spine, such as Pott's disease, bony exostoses, spinal-cord lesions, lumbago, neuralgia, etc., must be considered. We have not space to enter into a full discussion of all these diseases, many of which present certain symptoms similar to those of renal and ureteral calculus. The *x*-rays alone are usually sufficient to make a diagnosis positive, and careful physical, urinary, and cystoscopic examinations are of great value. It is well to lay stress upon the fact that chronic prostatitis and seminal vesiculitis are very frequently associated with pain in the back of a dull, aching character, and localized in the region of one or both kidneys. Not infrequently crises of pain occur in these cases exactly simulating renal colic, even radiating to the groin and testicle, and not infrequently associated with hematuria, irritability of the bladder, frequency of urination, pyuria, etc. The writer has seen a number of such cases, in which an operation had been performed upon the kidney, which was found to be normal. In all of these cases rectal examination showed an extensive chronic inflammatory condition around the prostate and seminal vesicle on the affected side. The hematuria and pyuria came from an inflamed posterior urethra, thus making the simulation of renal colic complete. Rectal examination,

stripping of the prostate and seminal vesicles, and the microscopic study of the secretion obtained will generally clear up the question at once. In all cases of pyuria careful search should be made for the tubercle bacillus, as this sometimes occurs with renal calculus. The differentiation between tumor and stone has been discussed elsewhere. It is often difficult to make a positive diagnosis without the x-rays. The cystoscope will generally show if the disease is vesical in character and careful examination of the spine should always be made.

**Treatment.**—When the urine of a patient is known to contain a considerable amount of certain salts, uric acid, oxalates, phosphates, etc., suitable treatment should be adopted to correct this condition. The use of water in abundance, and particularly certain mineral waters, such as those at Saratoga and Poland Springs, Vichy, Contrexeville, Evian, certain German spas, etc., is of value. Healthy exercise, with regular breathing and special diets, according to the salt present, are indicated. the use of hexamethylenamine, piperazine, benzoate and carbonate of lithia, etc., have been advised, as these may act as valuable solvents, but it is probable that diet, exercise, and water in abundance are the most valuable methods. When the calculus is formed and is apparently not too large to pass, the use of glycerin in large doses, 50 to 100 cc. daily, has been strongly advised; it is said to provoke painful crises and to be followed by expulsion of the calculus. The writer had success with this in one patient in whom a calculus lodged in the lower portion of the ureter. It is often surprising to find that very large calculi have been passed, and Leonard has taken the position that before operation is carried out every effort should be made to cause the passage of a small calculus. Casper has advised the injection of oil into the ureter, a method used by the writer with success in a few cases.

Dilatation of the ureter below the site of the lodgment of the calculus has also been successful. When the stone is lodged in the very end of the ureter it is sometimes possible to dislodge it with the ureteral catheter, or it may be possible to slit up the ureter by means of an operating cystoscope, and thus facilitate the escape of a calculus. In the female, vaginal massage or stripping from above downward sometimes pushes the calculus into the bladder, and rectal massage has also been advised in the male. Although renal and ureteral calculi may often remain for years without producing severe symptoms, this is not the rule, and usually they lead to very destructive processes. Even when the calculus is small its extraction should be undertaken when it has not been evacuated by protracted treatment. It has now been demonstrated that the operation of nephro- or ureterolithotomy is practically free from danger in uncomplicated cases, and that all portions of ureter are alike amenable to surgical treatment by an extraperitoneal operation, with the exception of the intramural and intravesical incarceration of calculi, in which the intravesical route (suprapubic or cystoscopic) is to be preferred.<sup>1</sup>

When the stone is lodged, and particularly when associated with

<sup>1</sup> See an article on the subject in the *Annals of Surgery*, May, 1903.



secondary infection, pyonephrosis, perinephritis, etc., operation should not be delayed. If the kidney is found to be in fairly good condition, nephrectomy usually need not be performed, and it is remarkable that the kidney, which is apparently considerably diseased, may often become quite useful and give no trouble after the removal of the calculus. When, however, there is extensive suppuration and the cortex is largely destroyed, the kidney should be removed if the condition of the patient warrants, and if the other kidney is healthy. The use of water in great abundance before and after all operations upon the urinary tract is the first principle. With the taking of large amounts of water, with saline infusions and slowly introduced enemata, uremia can be prevented even in severe renal disease. With anuria energetic efforts should be adopted at once to bring on urinary secretion—water in abundance, infusions, enemata, transfusions, sweat baths, cupping, diuretics, etc. Watson has shown that delay is very dangerous, and if the anuria persists after the use of active medical measures from twenty-four to forty-eight hours, an immediate and rapid operation should be carried out, with the object of incising the kidney and draining the pelvis. If the condition of the patient is dangerous, no attempt should be made to remove the calculus, unless this is very easily accomplished; a secondary lithotomy can be performed later. Casper has advised ureter catheterization and the injection of water or oil into the kidneys, with the idea of dislodging the stone and of stimulating renal secretion. This procedure has been successful, and may be used in appropriate cases; but it is not advisable to wait long before operation is carried out when the condition of anuria persists.

One important object is to prevent recurrences and diet should play a large part in this. Bradford<sup>1</sup> mentions three factors concerned in the formation of calculi: (1) Composition of food; (2) the amount of the particular calculus-forming ingredient in the urine and its chemical relationship with the other urinary constituents; (3) inflammation of the renal pelvis.

The formation of uric and oxalic acid stones does not depend wholly on the amount of these substances present in the urine. Yet, the amount may influence the formation of stones to some degree. Hence, the regulation by diet of the amount secreted becomes important. Where it is desirable to modify the reaction of the urine for a prolonged period, dietetic measures are more suitable than the administration of drugs. The excretion of uric acid cannot be prevented by any system of dieting. Yet, the deposition can be influenced by dietetic measures by restricting the output of uric acid and by altering the reaction of the urine. Approximately one-half the uric acid excreted is the result of metabolism of the tissues. For uric acid to remain in solution the urine must not be unduly acid and salts must be present to provide necessary bases to combine and form biurates. This is brought about by vegetable diet, inasmuch as vegetables are rich in alkaline salts, especially those of potassium.

<sup>1</sup> A System of Diet and Dietetics, edited by G. A. Sutherland, 1908, Chap. xxii.

In this way urine can be rendered less acid or even neutral and the deposition of uric acid hindered. The free ingestion of water is advised.

Conditions are different with calcium oxalate stones, as the great bulk of it in the urine is derived from foods or products of decomposition in the alimentary canal. It is probable that only traces of oxalic acid are formed in the tissues during metabolism. The formation of calculi composed of oxalates depends on other factors than the mere quantity excreted, as the process lies in the formation of relatively insoluble calcium oxalate instead of excretion of the soluble oxalate. Rhubarb and tomatoes have a high oxalic acid content and the ingestion of large amounts produce oxaluria. Oxalic acid is also found in the stomach in cases of dilatation with diminished hydrochloric acid by fermentation and decomposition. The regulation of diet is more important in the prevention than in the cure. No dietetic measures can affect stones already formed but may prevent the formation of subsequent ones. The dietetic treatment for *oxaluria* consists in the exclusion of foods containing abundance of oxalates. This must be combined with the treatment of the gastric disturbance.

Kahn and Rosenbloom call attention to the treatment of giving alkaline solutions to patients with stone disease, and to the necessity of changing the therapeutics in renal calculi, since the majority of these calculi are composed of the insoluble salts of calcium and not of uric acid or urates. They insist that the treatment of insoluble calcium salts is entirely different from that of uric acid. The antacid treatment should not be used in calcium stones. They conclude that calculi obtained by operation or otherwise should be subjected to analysis and if composed of calcium salts no antacid treatment should be advised. They further conclude that the majority of renal stones are composed of calcium oxalate and that sometimes the calcium salt is the only component of the stones.

## CHAPTER XXI

### GENITO-URINARY DIAGNOSIS. DISEASES OF THE PROSTATE

By HUGH HAMPTON YOUNG, M.D.

#### EXAMINATION OF URINE

METHODS ordinarily employed in the collection and examination of urine may lead to very grave errors in diagnosis. When all the urine is voided into one receptacle it is impossible to say whether certain pathological constituents may have come from the urethra, prostate, or bladder, but by making use of three receptacles much important data can be obtained. In a case of acute gonorrhœa, which is confined to the anterior urethra, if the patient voids urine in only one receptacle it will be cloudily with pus, but if he voids in three receptacles it will be clear in the second and third, due to the fact that the purulent secretions in the anterior urethra have been washed out by the first urine voided. If, however, the inflammation has passed the external sphincter in the triangular ligament and involved the prostatic urethra, the secretion which cannot escape anteriorly through the tightly closed membranous urethra passes upward into the bladder and mixes with the bladder urine. In such cases the urine voided in three glasses shows pus in all three, and cannot, therefore, be differentiated from pus arising from the bladder or kidneys. Blood coming from the anterior or posterior urethra follows the same directions as purulent secretions. In some cases of hematuria from the prostatic urethra the bleeding does not occur except at the end of urination, when the final spasm squeezes out the blood from the inflamed or ulcerated verumontanum or middle prostatic lobe. In a similar way purulent secretions which lie in the prostatic ducts in chronic prostatitis often appear as shreds in the last urine voided. In cases of spermatorrhœa, spermatozoa likewise are present in large numbers in the last urine. By the use of the three glass tests a fairly accurate differentiation of the various portions of the urethra is obtained and the origin of many a case of albuminuria, hematuria, or pyuria is explained.

It is important that the urine should be examined soon after voiding, and for this purpose every physician should have a centrifuge, microscope, two or three staining fluids, and the simple apparatus necessary for a fairly complete urinalysis. When the urine is allowed to stand there is a rapid growth of bacteria and in a short time a precipitate which often obscures the presence of tube casts or other pathological elements. On this account urinary infections are often completely overlooked. It is particularly important in cases in which instrumentation of the urethra or bladder has been carried out to watch the urine for bacterial



infection, and when, in such cases, the third glass of voided urine shows a cloudiness, it should be examined at once. The passage of urine through the urethra generally washes out all the bacteria which it contains, but if cultures are wanted, or if the diagnosis between the smegma bacillus and the tubercle bacillus is desirable, the anterior urethra should be thoroughly cleansed by irrigation with sterile water, and the penis (particularly the foreskin, glans, and coronal sulcus) cleansed with soap, water, and 1 to 1000 bichloride of mercury solution. If this is done and the urine is voided in three sterile receptacles, the third urine should always be free from extraneous bacterial infection, and if bacteria answering the description of the tubercle bacillus are found, one can be quite positive that tuberculosis is present.<sup>1</sup>

The effect of bacteria upon the secretion of urine and the production of urinary precipitates is very great. Certain bacteria, particularly those of the proteus group, have a very marked alkalizing effect and cause a rapid deposition of phosphates and the production of calculi. Most ammoniacal urines are due to this bacillus. Some of the staphylococci render the urine alkaline, but they are generally less rapid and intense in their action. Other bacteria, notably those of the colon group, never lessen the acidity of the urine, but in some cases add to its acidity. When bacteria of different effect (alkalinizers and acidifiers) are present they seem to neutralize each other, and with the preponderance of one or the other the reaction of the urine is found to change.

Bacteria are not infrequently present in the urine in large numbers in cases in which there is no pus to be found, and the writer has seen numerous cases of persistent bacteriuria in which no signs of inflammation developed, and only by immediate examination of the urine, voided in three glasses, would the condition have been detected. Such an examination is important in many of the acute febrile conditions, owing to the not infrequent development of bacteriuria and pyuria, and is now well recognized in typhoid fever.

**Instrumental Examination.**—It may not be amiss to say a few words in regard to the use of the simpler exploratory instruments.

FIG. 14



Bougie with olive-shaped ends.

**Bougies.**—Bougies are of great value in detecting the presence of stricture of the urethra. The best instruments are made of silk or linen covered with gum and provided with an olive-shaped ball at one or both ends, as shown in Fig. 14. The general practitioner should have at least four of these instruments, varying in size from 14 to 26, French scale. They cannot be boiled, and should be cleansed with soap and water and by immersion in 1 to 1000 bichloride of mercury. For stricture of the deep urethra, curved metal sounds are necessary. One should have at least six of these varying in size from 20 to 30, French; they are

<sup>1</sup> For further discussion, see *Johns Hopkins Hospital Reports*, 1906, vol. xiii.

sterilized by boiling. In their introduction care should be taken, particularly in passing through the membranous urethra, not to produce traumatism, false passage, etc. After the beak has passed into the bladder the instrument may be used as a searcher for calculi. If a No. 28 French passes, the urethra can generally be said to be free from stricture.

**Catheters.**—There is probably no instrument with which more harm has been done than the catheter, and on this account a word of caution seems advisable. In the great majority of cases in which a catheter is necessary, prostatic hypertrophy is producing the obstruction. In such cases the urethra is distorted not only by the pressure of the lateral lobes, but by the upward growth of a median lobe, which usually produces an acute flexure in the floor of the urethra. The size of the ordinary silver catheter or straight catheters of gum or rubber has led to the tunnelling of this median portion of the prostate in thousands of cases, and the pathological museums contain many beautiful specimens but sad reminders of disaster. By the use of the coudé (or elbowed) gum-linen catheter, catheterization can be successfully performed without injury in almost all cases of obstruction to urination from prostatic hypertrophy. The acute bend in the instrument, shown in Fig. 15, enables it to ride

FIG. 15



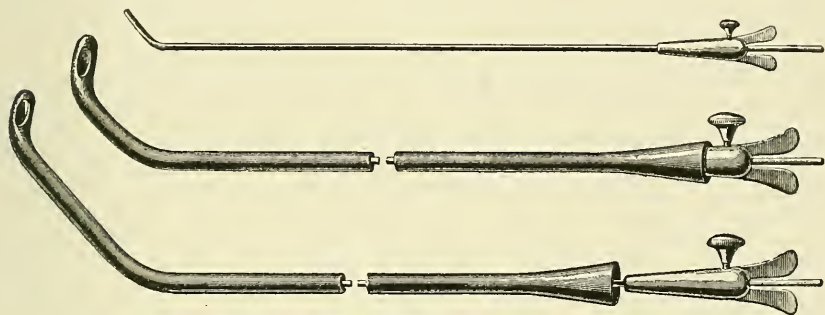
Coudé catheter.

over the obstructing barrier in the median portion of the prostate. This instrument is indeed the most satisfactory for general use, and should be recognized by the profession as the standard catheter to be first employed in nearly all cases. The straight rubber catheter, which is now almost exclusively employed, is often difficult to introduce in normal cases, owing to the fact that its point becomes engaged either in the pouch of the bulb just at the external sphincter at the median portion of the prostate, or in front of the external sphincter. The shape of the coudé catheter, on the other hand, enables it to escape being caught in either of these natural depressions. The straight rubber catheter, however, has its place, and is particularly useful in cases of cancer of the prostate, in which it is much more easy to introduce than the coudé catheter. The silver catheter is also of importance, but should usually be employed only when the coudé or the rubber catheter has failed, and great care should be taken to avoid making a false route. In cases of prostatic hypertrophy a special silver catheter with a large "prostatic curve" is often of help, and the two stilets which were invented by Guyon, Fig. 16, enabling one to give almost any curve to gum or rubber catheters, are often of great assistance.

For cases in which retention of urine is caused by a definite stricture,

a catheter which can be attached to a filiform is often of great value, the filiform leading the catheter through the strictured portion of the urethra. As it is impossible in some cases to introduce any form of instrument, an aspirating apparatus should always be at hand. The needles employed should not be any larger than the average steel bonnet-pin. Aspiration may be repeatedly done with these without much danger and with practically no fear of extravasation.

FIG. 16



Guyon's stilet to facilitate introduction of catheter in prostatic hypertrophy.

**Asepsis.**—Before attempting any urethral instrumentation great care should be taken to prevent infection. The penis should be thoroughly cleansed with soap and 1 to 1000 bichloride of mercury, and should be surrounded with a sterilized towel saturated with the same solution. The anterior urethra should be irrigated with 1 to 60,000 bichloride of mercury, and the operator's hands cleansed with soap, water, and bichloride of mercury, or other approved methods, before any attempt to introduce the previously sterilized instruments is made. Great care should be taken to avoid traumatism, and the bladder should be irrigated with a solution of 1 to 60,000 bichloride of mercury, or 1 to 10,000 nitrate of silver before the instrument is withdrawn. Usually the patient should take some internal urinary antiseptic (such as hexamethylenamine, 45 to 60 grains a day) for several days after the procedure (and if possible before also), and careful examinations of the urine, voided in three glasses, should be made on subsequent days in order to detect the occurrence of infection. If this were done by all practitioners, many of the disastrous results of urethral instrumentation would never occur. It is the rarest thing to find physicians properly equipped with even the instruments absolutely necessary for emergencies, such as they are apt to meet at any time, and on this account it seems desirable to give a list of genito-urinary instruments which should be in the possession of every general practitioner.<sup>1</sup> But if the physician is able to invest in only

<sup>1</sup> Glass urethral nozzles for antiseptic irrigation of the urethra and bladder. Sounds for dilatation of the urethra (Nos. 18, 20, 22, 24, 26, 28, French). Filiforms, for strictures of small calibre, with screws for attachment to dilating followers (Nos. 10, 14, 18, 22, French). Catheters: coudé prostatic gum silk catheters which can be boiled (Porgès) (Nos. 14, 16, 18, French). Rubber straight "Nélaton" catheters (Nos. 10, 14, 16, 18, French). A silver van Buren curve (No. 16, French). Guyon's stilets, coudé and Béniqué curves (to give a proper curve to gum and rubber catheters).



one instrument, let it be a coudé gum catheter, and one that can be thoroughly sterilized by boiling (such as the French make of Porgès).

**Visual Exploration.**—The use of the urethroscope and cystoscope has become so greatly popularized of late that a few words may not be amiss. Here, too, great care should be taken to avoid infection, and on this account a urethroscope, in which the light is not carried in the tube of the instrument, but is thrown in from without, is much to be preferred. By its use diagnoses of obscure urethral lesions can occasionally be made. The topical treatment of chronic gonorrhœa and diseases of the verumontanum is often of very great benefit. Cystoscopy is performed with the bladder distended with water or with air.

It is impossible here to discuss the advantages and shortcomings of both these methods, but suffice it to say that, for general diagnostic work, thorough inspection of the entire bladder, study of the action of the two ureters and of the size and distribution of the prostatic lobes, the simple cystoscope of Nitze with the bladder distended with water is by far the best instrument. This little instrument, with its coudé beak, is one of the easiest to introduce, and with the use of novocain in the urethra its employment is rendered extremely simple and free from pain. Its findings are usually so certain, and often so brilliant, that it seems remarkable that it is not now used with far greater frequency. With the simple cystoscope it is possible not only to distinguish between the various diseases of the prostate and bladder, but also by study of the ureteral orifices to give an accurate interpretation of the condition of the two kidneys in many cases.

Renal hematuria or pyuria can easily be detected by watching the intermittent outflow of urine from the ureteral orifices, and in many cases of unilateral renal disease a pathological condition of the lower end of the ureter can be detected.

For intravesical treatment in the female the use of an open tubular cystoscope and vesical distension with air is generally to be preferred, as successfully used by H. A. Kelly. Catheterization of the ureters is no longer a difficult procedure, and can usually be accomplished with very little pain after the use of novocain (5 per cent. solution) in the urethra. The writer's preference is for the catheterizing cystoscope, made by Wappler in New York, which is provided with two catheters, and at the same time is of small size, so that its introduction is not difficult. Ureteral catheterization has not become so easy that it is to be recommended as a routine procedure by all practitioners. It can be learned, however, without great difficulty, and it should be employed much more widely than it is. By the use of formalin vapors, thorough sterilization of the ureter cystoscope and catheters can be obtained and the dangers of vesical and ureteral infection can be reduced to almost *nil*.

By the introduction of the phthalein test, Rowntree and Geraghty have given an accurate and simple method of determining the functional value of one or both kidneys.

## THE DIAGNOSIS OF CERTAIN GENITO-URINARY AFFECTIONS

**Urethritis.**—The characteristics of the gonococcus are so well known today that it would hardly seem necessary to say anything in regard to diagnosis; but very little is generally known about the so-called pseudogonococci and the persistence of gonorrhœa without gonococci.

In an acute urethritis with a profuse discharge of pus the gonococcus is usually found so quickly and in such great numbers that a positive diagnosis is easy. When, however, the discharge is slight, or the only purulent secretion present is found in the shape of shreds in the urine, the detection of the gonococcus is often very difficult. This is due first to the presence of other organisms which closely simulate the gonococcus. Some of these do not decolorize by Gram, although they are typical in shape and intracellular; but there are others in which the organism is not only a biscuit-shaped diplococcus, but also decolorizes by Gram. Fortunately, the latter organism is found very rarely in the urethra (according to See, in a proportion of 2 per cent. of the bacteria found in the normal urethra). These pseudogonococci are non-pathogenic and are found only in very small numbers, so that if the rule is made to make a positive diagnosis of the gonococcus only when present in fair number, and when located within the pus cells, no mistake will be made, according to See. But the absence of the gonococcus is not sufficient to warrant the assertion that the case is non-infectious. In the majority of cases of chronic gonorrhœa it is almost impossible to find the gonococcus or in fact any organism, but multitudes of cases of pelvic inflammatory trouble in women prove the fallacy of the idea that these patients cannot transmit infection.

The absence of the gonococcus is not the all-important question. Of course, whenever the gonococcus is present the condition is far from cured, but because it cannot be found or even because there is no evidence of a urethral discharge is no justification for the habit of telling the patient that he is cured. Before a gonorrhœal patient is discharged as well he should undergo a careful routine examination, which should include examination for discharge at the meatus, and shreds in the urine, voided in three glasses; palpation of the prostate and seminal vesicles; expression of their contents for microscopic study and the examination of the urethra with a sound for infiltrations, strictures, etc. As long as urethral shreds composed largely of pus cells are present the patient cannot be considered well. As long as the prostate is enlarged, indurated, and the secretion contains pus cells in considerable number there is great danger to the opposite sex. The fact that a marked prostatitis may be present, when there is no evidence of chronic urethritis at the meatus or in the urine, shows the very great importance of a routine examination of the prostate and seminal vesicles, and even when the prostate feels normal it is important to examine its secretion, which can easily be made to appear at the meatus simply by vigorous massage. The normal secretion is largely composed of lecithin cells easily recognized, and the presence of a definite number of polynuclear leukocytes, as shown by the addition of acetic acid, demonstrates

at once the presence of a chronic inflammatory condition of the prostate. Fortunately, this condition is generally curable by a prolonged course of prostatic massage and other local treatment, but until such cure is effected, marriage is generally a hazardous procedure, even if repeated careful examinations fail to show the gonococcus. The gonococcus fixation test, if positive, should prevent marriage. If negative we cannot say that a gonococcus infection is not present.

**Chronic Prostatitis.**—The importance of chronic prostatitis, which is one of the most common diseases with which the adult male is afflicted, and the fact that it is responsible for symptoms in regions far remote and simulates many other affections, is very little appreciated. The symptoms of chronic prostatitis may be sexual, urinary, or referred. Only the last is discussed here, as we have not space to write of the numerous sexual disorders or to the urinary irritations and obstructions produced by chronic prostatitis. The referred symptoms are of a painful nature, and may involve the back, hips, thigh, rectum, perineum, groins, and scrotum. They seem to occur in four distinct groups: (1) Those involving the rectum, perineum, and urethra; (2) those involving the groin and scrotum; (3) those following the course of the sciatic nerves and involving the legs, thighs, hips, and buttocks; and (4) those involving the back and region of the kidneys.

These referred pains are generally of a dull, aching character, coming on at certain periods of the day; in some cases painful seizures of considerable intensity occur. This is particularly true of those cases which simulate renal colic, often being of such severity as to require morphine. They are often accompanied by hematuria and marked irritability of the bladder (both due to an inflamed prostate), and the simulation of the symptomatology of renal calculus is often perfect. Rectal examination in these cases usually shows a marked inflammatory infiltration, involving the prostate, seminal vesicle, and surrounding structures in the pelvis on the side in which the pain occurs. The explanation of these referred pains is, according to Head, that a painful stimulus received at an internal organ is directed upward to that segment of the cord from which its sensory fibres are given off; there it comes in close communication with the fibres from the surface of the body which arise from the same segment, and thus the pain is referred to another region than that of the viscera actually affected. The prostate receives fibres from the tenth, eleventh and twelfth dorsal, the first, second and third sacral, and the fifth lumbar segment. With this varied distribution it is easy to see how the referred pains occurring as a result of chronic prostatitis may simulate, as they do, lumbago, nephrolithiasis, coxalgia, sciatica, varicocele, and other conditions in the various regions from the diaphragm to the toes. It is safe to say that chronic prostatitis is responsible for many of the so-called neurasthenias in the male, and that many painful maladies which go untreated could easily be recognized if careful examination were made of the prostate and its secretion.<sup>1</sup>

<sup>1</sup> Those who are interested will find an extensive report of cases in the *Johns Hopkins Hospital Reports*, 1906, vol. xiii, and articles by McCrae and the writer in the *Jour. Amer. Med. Assoc.*, 1913, vol. lxi, pp. 477 and 822.



McCrae, in drawing attention to the remote effects of lesions of the prostate, has emphasized the frequency of general nervous disturbance due to this cause. There are also many disturbances of the circulation. Some of these are evidently functional in character and specially characterized by attacks of palpitation of the heart and sometimes by pain so severe that angina pectoris is diagnosed. In many of the patients with chronic prostatic disease there is serious involvement of the myocardium, and the rapid improvement which may follow prostatectomy is remarkable. A phlebitis sometimes occurs, apparently secondary to prostatic infection. The possibility of the prostate being the source of infection in cases of arthritis deformans should be kept in mind.

It is very important for practitioners to make a routine examination of the prostate as a regular part of physical examination in order that they may become adept in recognizing slight changes in the gland and its adnexa. With the patient bending forward with his elbows upon his knees, the index finger (covered with a rubber cot) is inserted into the rectum, and systemic examination of the membranous urethra, prostate, seminal vesicles, and vasa deferentia made. With practice, no difficulty is usually experienced in mapping out these structures and in determining pathological changes. In *chronic prostatitis* the prostate is often somewhat enlarged, irregular, sometimes nodular, with induration in places, and at times great tenderness. It is apt to be associated with an induration along the vasa deferentia and lower portion of the seminal vesicles, and continuous with that of the prostate. In some cases the seminal vesicles are enlarged and indurated, and the space between them may be filled up by a broad plateau of infiltration which connects the indurated vesicles. Adhesions to the pelvic wall on one or both sides, fixing the prostate and sometimes the seminal vesicles, are a fairly common finding, the periprostatic infiltration occasionally being very extensive. In some cases the prostate appears normal; it is impossible to make out any enlargement, irregularity, or induration, and the great importance of obtaining some of the secretion by massage or stripping of the seminal vesicles or prostate is evident. This stripping process, carried on systematically from above downward, soon empties considerable secretion into the prostatic urethra, from which it may be carried by a similar stripping movement through the external sphincter, after which it runs down freely to the meatus, where it may be caught upon a slide for microscopic examination. In normal cases the prostatic secretion is composed largely of lecithin cells, which are small, translucent, non-nucleated bodies, varying in size from that of a blood-platelet to that of a red-blood corpuscle. Large granular cells, epithelial cells, and spermatozoa are also seen. If trauma has been produced, red and white corpuscles may be present. Often by the microscopic examination alone the presence of a prostatitis is recognized. The writer strongly urges the necessity of this examination as a routine.

Chronic prostatitis is essentially a periacinous infiltration. The accompanying processes in the seminal vesicles and in the periprostatic and perivesical tissues are much the same. In these processes the nerve terminals, fibres, and ganglia are frequently involved, and to this is due

the many referred pains which occur. The purely sexual symptoms are most often due to changes in the verumontanum, characterized by infiltration, enlargement, congestion, and dilatation of the ejaculatory ducts. The urine in these cases is apt to show fine comma shreds in the third urine voided, due to the squeezing out of purulent plugs or moulds from the lumina of the prostatic ducts during the last spasmodic efforts of urination. Spermatorrhœa may be present also.

In a study of 358 cases of chronic prostatitis the symptoms were as follows: Frequency of urination, 90 cases; pain during urination, 46; urgency of urination, 25; difficulty of urination, 11; irritability of the deep urethra, 11; pain at the end of urination, 7; pain at the beginning of urination, 3; and dribbling after urination, 1. In 34 cases definite obstruction to urination was present, but in only two cases was the retention of urine complete. These men were thirty-two and thirty-seven years of age, and one had led a catheter life for twelve years. (These patients were cured by perineal prostatectomy.) The location of the referred pains was as follows: Lumbar region, 64; region of the kidney, 8; of a colicky nature simulating renal colic, 10; in the perineum, 35; suprapubic, 22; groin, 18; urethra, 14; rectum, 13; thighs, 12; hips, 10; sacrum, 5; simulating sciatica, 5; knees, 4; and legs, 4.

In some cases these painful seizures were of great intensity. This is particularly true of those cases which simulated renal colic, the attacks being of such great severity as to require morphine. These attacks are not infrequently accompanied by hematuria and marked irritability of the bladder (both due to posterior urethral inflammation), so that the simulation of renal colic due to calculus is often perfect, and in six of the ten cases exploratory operation had been performed on the kidney without finding a calculus. Rectal examination in these cases usually showed a marked prostatitis, with infiltration around the seminal vesicles and adhesions to the pelvic wall. The treatment of these cases is most satisfactory, and consists in prostatic massage, very hot rectal douches given with Martin's rectal tube, local application of nitrate of silver to the verumontanum and posterior urethra, intravesical irrigations, dilatation, etc. Frequently extensive infiltration of very chronic character and involving apparently the whole floor of the pelvis disappears under this treatment, with an immediate amelioration and the final cure of symptoms of long duration. Drainage of the seminal vesicles (and prostate) has been shown to yield remarkably good results in severe chronic inflammatory conditions of these organs. Before a diagnosis of neurasthenia in the male is made a most careful examination of the prostate and seminal vesicles and their secretion should be made.

**Tuberculosis of the Genito-urinary Tract.**—With an insidious hematuria or pyuria the suspicion of the presence of tuberculosis in some portion of the urinary tract generally arises. Owing to the fact that tuberculosis is very rarely primary in the bladder, it is important to recognize the original focus of the infection. Although the bladder is infected in the majority of cases, the primary site is generally in the kidney, the prostate and seminal vesicles, or the epididymis, and in many cases all of these structures ultimately become involved. In

cases of tuberculosis of the epididymis, prostate, and seminal vesicles, palpation will generally make the diagnosis clear; but in some cases the differentiation between tuberculosis and a chronic inflammatory condition is not easy, and it is important to find the bacilli. As remarked above, if care be taken to cleanse the penis, irrigate the anterior urethra, and collect the urine in three sterile glasses, one can be positive that an organism obtained from the third urine which answers the proper staining tests is the tubercle and not the smegma bacillus. In many cases it is advisable to determine the extent of vesical involvement and the presence of tuberculosis of either kidney, and for such the cystoscope is very necessary. Fortunately, by ureteral meatoscopy (a term invented by Fenwick to designate a simple inspection of the ureteral orifices) it is possible to form some idea of the condition of the kidney on that side. If tuberculosis is present the fluid ejected will be cloudy, and perhaps show a large amount of muco-pus, and the mucous membrane surrounding the orifice will usually show marked inflammatory changes, varying from hyperemia and œdematous swelling to severe ulceration. Ureteral catheterization should always be carried out if possible and can usually be done unless the bladder be too irritable or contracted.

Before the performance of nephrectomy one should be absolutely certain that the other kidney is functioning. It is needless to say at this date that the various segregators are absolutely unreliable, especially in cases of tuberculosis.

**Hypertrophy of the Prostate.**—According to Sir Henry Thompson, one man in every five over fifty years of age suffers from prostatic hypertrophy. Many of these cases never cause much trouble, but the great frequency of the disease, and the fact that it is first seen by medical men, warrant a few words upon the subject.

Prostatic hypertrophy usually consists of many spheroids of hypertrophic gland tissue bound together in a fibrous stroma, the whole forming an encapsulated lobular mass, which presses against the urethra and may extend far into the bladder. In 120 specimens examined by us, 100 were of the glandular type, 14 of the fibromuscular, and 6 inflammatory. Besides the enlargements of the lateral lobes, a more or less considerable hypertrophy of the median portion of the prostate, the so-called middle lobe, which lies beneath the urethral orifice at the vesical opening, is very commonly present. This produces by its growth a bar at the neck of the bladder, which acts not only as an obstruction to the outflow of urine but to the introduction of a catheter. In nearly all such cases there is an acute bend in the urethra, sometimes with a formation of a pouch in front of this median bar or lobe. This is also often associated with a contracted condition of the prostatic orifice, so that the introduction of a straight instrument is in many cases impossible.

The usual results of prostatic obstruction are, at first, frequency of urination and a gradual contracture of the bladder, with progressive lessening of its capacity. Later, the bladder is not completely emptied, and the residual urine gradually increases. Complete retention



of urine sets in, as a rule, without warning, and, in some cases, when there has been very little difficulty of urination. Often the passage of a catheter will be followed by a complete retention of urine, which may not disappear until operation is performed. The bladder usually becomes trabeculated, and pouches and diverticula form, in some cases reaching great size. Dilatation of the ureters and renal pelvis is often present to a marked degree when the symptoms do not suggest any such changes, and if an ascending infection occurs the case at once assumes a desperate character. The symptoms are usually those due to gradually increasing obstruction, viz., hesitation, straining, increased frequency of urination, with smallness of the stream, and often several isolated attempts or efforts are required before the act of urination is completed. With increase in the residual urine, urination gradually becomes more frequent and difficult, and in most cases complete retention and a catheter life ultimately results. In rare instances the bladder may become very greatly distended, and although there is much residual urine (from 1000 to 5000 cc.), the overdistended bladder may be able to functionate apparently quite normally, voiding large amounts of urine at long intervals, so that one is surprised to find a greatly distended bladder with a large amount of residual urine. In other cases incontinence, generally with considerable residual urine, is present. The varied symptomatology cannot be discussed in detail, but we wish to lay stress upon the fact that often with few symptoms present very serious destructive processes are going on, and, almost without warning, the patient is often found to be in a desperate condition. The great importance of instituting treatment early, before the occurrence of a large amount of residual urine and before the formation of diverticula and hydro-nephrosis, is shown by the fact that in early cases operation is practically free from danger, whereas in the latter class of cases there is always danger of uremia, although it is possible with careful treatment to help nearly all of these patients.

As remarked above, a special coudé catheter should be employed in cases of prostatic hypertrophy, because the abrupt curve near the point of the instrument enables it to ride up over the median bar. The use of straight rubber catheters, and even the ordinary silver catheter, is, as a rule, dangerous, and the straight olive-tip pointed silk catheter should never be used.

The question as to what is the proper treatment to follow when the patient comes into the hands of the practitioner is of great importance. It is well recognized that a large amount of residual urine should never be allowed to continue indefinitely, owing to the injurious effect upon the higher urinary organs, and on this account many have advised systematic catheterization when the amount of residual urine is larger than 150 cc. Unfortunately, the first catheterization is not infrequently followed by complete retention of urine, necessitating the beginning of a catheter life, and on this account, when one considers catheterizing for the first time, he must always be prepared for such a result. It is not safe to withdraw residual urine and leave the patient thinking that he will be able to void as before; and as frequent catheterization is almost

always followed by infection of the bladder, cystitis, etc., the question of the employment of the catheter is a serious one. The use of a catheter, even in the hands of skilful patients, with abundant means at hand to perform it properly, is frequently beset with great difficulties and serious complications, such as false passages, catheter fever, prostatic abscess, unrelieved retention, with increased dilatation of the ureters and kidneys, ascending infection, etc. The breakdown of catheter life occurs in a large percentage of the cases before many months have passed, and a surgical operation is then often required in an emergency to save life. On the other hand, the surgical treatment of prostatic hypertrophy has progressed rapidly, and the operation of prostatectomy has now become remarkably simple and free from danger, even though the surgeon is still required to treat many patients who have suffered from the disease for a long time and are in serious condition on account of numerous complications. The operative mortality of perineal prostatectomy varies from 3 to 6 per cent. in the various statistics, and of suprapubic prostatectomy from 6 to 10 per cent.

Owing to the terrible suffering of some of these unfortunate patients, operators have been induced to do the operation upon desperately ill and very aged men, and this fact is largely responsible for the presence of any mortality. For example, the writer has had 12 deaths following 350 cases of perineal prostatectomy. About 30 per cent. of these patients were over seventy years of age and 12 over eighty years of age, and among the 12 deaths, 5 were over eighty years. The writer had (from July 24, 1905, to March 20, 1908) 128 consecutive cases of perineal prostatectomy without a death, every patient leaving the hospital well or improved. Four of these patients were over eighty years of age, 19 between seventy-five and seventy-nine, and 22 between seventy and seventy-four. Many of these patients, besides being very aged, were in poor physical condition. In 20 cases more or less severe organic heart disease was present (dilatation, endocarditis, myocarditis, and arteriosclerosis). In 6 cases pyelitis or pyonephrosis, in one case renal calculi, and in another ureteral calculi were present. These statistics are mentioned to show that there was no choosing of the cases, and that the operation of conservative perineal prostatectomy is a satisfactory one.

It seems evident, therefore, that all patients with prostatic hypertrophy and gradual increasing obstructive symptoms should be subjected to operation before serious complications arise. The use of a catheter even for a protracted period is not to be advised, as it almost invariably results in infection, which is often very difficult to remove. When, however, the amount of residual urine is large, say 400 to 2000 cc., frequent catheterization should be carried out for a protracted period before operation, so as to allow the distension of the ureters and kidneys to be relieved. In some cases it may be advisable to fasten a retained catheter in the urethra, and it is remarkable how such drainage leads to a rapid improvement of the function of the kidneys. In numerous instances severe uremia has cleared under this treatment (water in large amounts by mouth, by rectum, or by infusion being given at the same time).

In such cases rapid improvement in the urine is noted (the phthalein test is an accurate index of this) and, as a rule, operation should not be undertaken until this improvement has been sufficiently marked to indicate that there is very little danger of renal suppression after operation. When catheterization is necessary the patient should be instructed to do it with proper antiseptic precautions, and he should be provided with coudé gum-silk catheters of various sizes. All such patients should take hexamethylenamine (from 15 to 40 grains daily—gm. 1 to 2.6) to prevent urinary infection. The medical man, however, is not justified in allowing his patient to adopt a catheter life unless the patient refuses operative treatment.

**Cancer of the Prostate.**—Recent statistics have shown that this disease is far more common than previously supposed. In five years in the writer's private practice there were about 250 cases of benign prostatic hypertrophy and 68 cases of carcinoma of the prostate—the proportion between cancer and hypertrophy was therefore 1 to 4. The rectal findings in carcinoma are usually so different from those of hypertrophy that there is no difficulty in diagnosis. In half of the cases cancer is not associated with hypertrophy of the prostate. The prostate is often much larger than normal, but it may not have any of the large rounded adenomatous lobes found in hypertrophy, and there is usually no intravesical outgrowth of lateral or median lobes unless there be a coexistent hypertrophy. The cancer begins most often beneath the urethra, and from here grows along the ejaculatory ducts, finally involving the space between the seminal vesicles beneath the trigone, from which it may in some cases invade the bladder. Slight elevation of the median portion of the prostate is not infrequently present, but rarely in the shape of a rounded intravesical lobe, as remarked above. In about 50 per cent. of the cases adenomatous hypertrophy of the lateral lobes, which may project into the bladder, is present, with a layer of carcinoma behind it, and just beneath the capsule of the prostate. The so-called malignant degeneration in previously benign prostates occurs very seldom, in the writer's opinion, and one should almost always be able to recognize carcinoma either by examination or at operation before the prostate has been removed.

The *symptoms* of cancer of the prostate are unfortunately very similar to those of hypertrophy. In a study of 87 cases seen by the writer, 50 per cent. occurred during the seventh decade, and only one case before the age of fifty. The first symptoms were usually frequency of urination, sometimes associated with difficulty and occasionally burning in the urethra. In 13 cases the first symptom was pain, located in the penis in 5, in the bladder in 4, in the thigh in 4, in the testicle and groin in 3, in the hip in 3, in the pubes twice, rectum once, legs once, and back twice. The pain was usually slight, but in some cases severe, and in some the diagnosis of rheumatism, neuralgia, sciatica, and lumbago had been made. Hematuria was the symptom at onset in only 4 cases. In one case the only symptom was swelling of one leg. The frequency and difficulty of urination are similar to that seen in prostatic hypertrophy. Retention of urine with a catheter life not infrequently comes on.



Hematuria is no more marked than in hypertrophy, but, as a rule, pain is a much more prominent symptom, especially in the later stages.

The *diagnosis* of carcinoma of the prostate is easy in the later stages, when the large stony mass of induration, involving the prostate, seminal vesicles, and intervesicular region, is present. When, however, the disease is still confined to the limits of the prostatic capsule, diagnosis is much more difficult. Examination of the writer's patients showed that cancer was almost always associated with a stony induration of part or all of the prostate. On cystoscopic examination there were generally no intravesical lobes, except when hypertrophy existed, and when the suburethral portion of the prostate was examined with the finger, while the cystoscope was still in the urethra, it was almost invariably found to be more thickened and indurated in carcinoma than in hypertrophy. A markedly indurated prostate in a man over fifty years of age should always be viewed with suspicion and, unless carcinoma can be excluded, should be subjected to an early exploratory prostatectomy. When the posterior surface of the prostate is exposed through the perineum it is usually possible, by palpation and inspection, to recognize carcinoma. In some cases, however, it has been necessary to make an incision into the prostatic lobes and excise a piece of tissue for frozen sections and microscopic examination. This procedure can be carried out in ten minutes, and if the disease is benign the ordinary enucleating prostatectomy can be carried out; but if malignant and no high infiltration is to be felt, a radical excision should be adopted.

A study of the pathology showed that in order to obtain radical cures it would be necessary to excise not only the prostate with its capsule and urethra but also the seminal vesicles and lower portion of the vesical trigone (the defect is easily closed by anastomosing the bladder with the membranous urethra). This operation the writer carried out in 9 patients. The results have been very gratifying and the prospects of a permanent cure are excellent in 6 patients, 2 of whom have lived over five years apparently without recurrence. The treatment of advanced cases may be divided into three classes:

1. Those in whom urination is not extremely frequent or painful. Here a let-alone policy is usually advisable. The patient should be told not to let the bladder become overdistended.

2. Those in whom urination is frequent and the amount of residual urine is large. In such cases the use of a catheter often gives great relief and removes the danger of renal complications from back pressure. A straight rubber Nélaton catheter (the ordinary red rubber catheter) is usually the best to employ, and several sizes should be at hand; but the largest that can be comfortably passed should be used so as to keep the posterior urethra somewhat dilated. In most cases the coudé prostatic gum catheter does not pass easily—the beak catches in the prostatic urethra, which is usually strictured and not merely compressed, as in hypertrophy. A silver catheter should be employed only when others fail, and then with great care.

3. Those in whom catheterization is difficult or painful. In these cases operative relief is generally necessary, and suprapubic drainage

may be employed. This necessitates the wearing of some form of apparatus. In some cases the patient gets along fairly well.

The Bottini electro-cautery operation may be used, and in some cases the results have been brilliant and permanent, the patient being able to void urine with fair comfort until the end.

A conservative partial perineal prostatectomy may also be done, the object being to remove the obstructive pressure of the lateral and median portions of the prostate. The writer has employed this operation in more than 60 cases, with excellent results. Several patients have lived three years, and had no return of the obstruction to urination. In about 70 per cent. of the cases the functional results have been as good as are obtained in benign hypertrophy of the prostate, urination being practically normal, and continuing so as long as the patient lives. I now carry out a conservative perineal prostatectomy instead of subjecting these patients to a catheter life.

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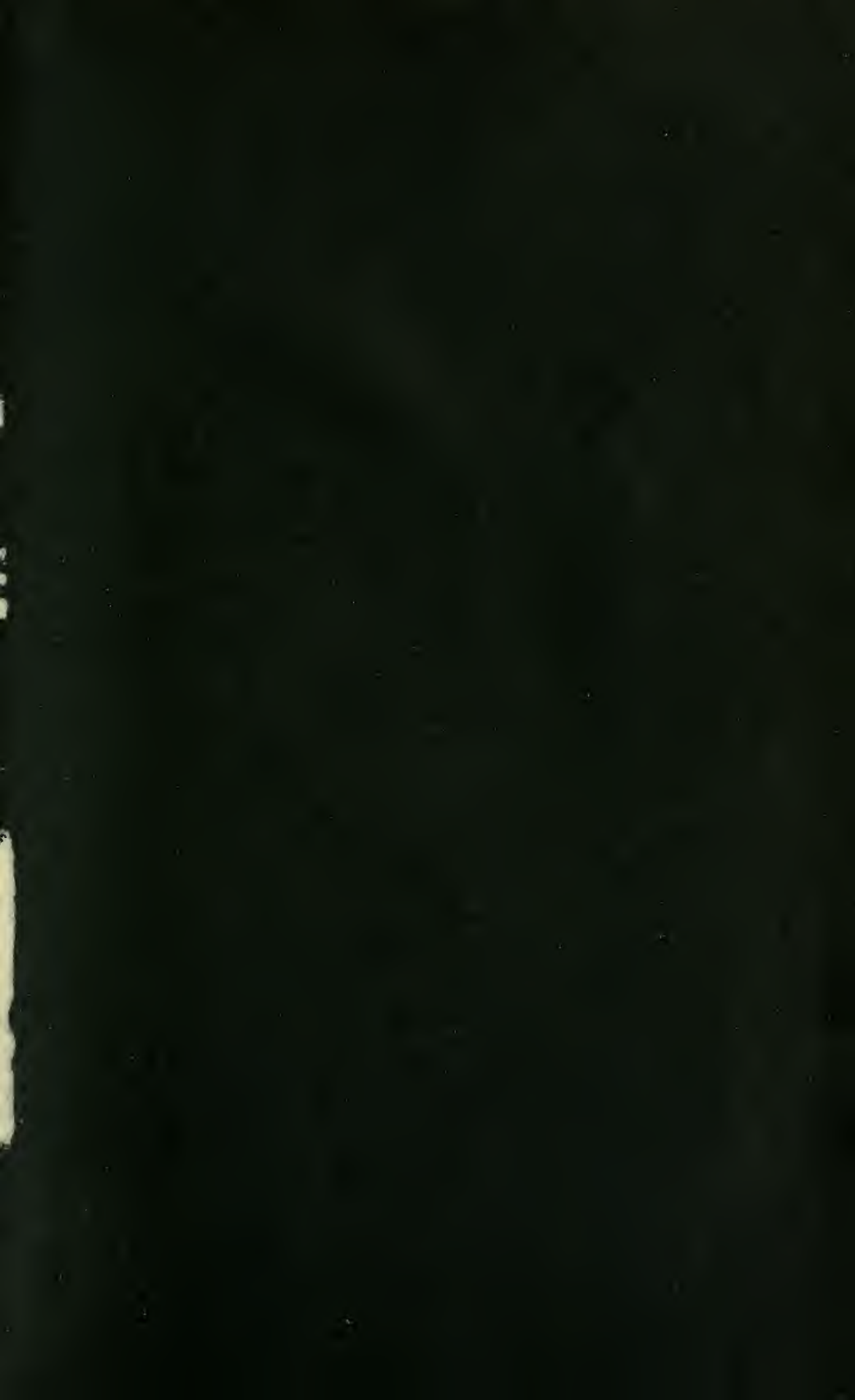
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